

# Cutaneous Polyarteritis Nodosa Treated with Pentoxifylline and Clobetasol Propionate: A Case Report

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## Abstract

Cutaneous polyarteritis nodosa is a rare type of cutaneous vasculitis. It affects the small- and medium-sized arteries of the dermis and subcutaneous tissue without extracutaneous involvement. The diagnosis is by skin biopsy, and the characteristic finding is a leukocytoclastic vasculitis. The authors report a case of a 14-year-old Saudi girl who was referred to the dermatology department because of multiple ulceronecrotic lesions on the frontal aspects of the distal lower limbs. She had past medical consultations and treatment, but without improvement. Histopathology confirmed the clinical diagnosis of cutaneous polyarteritis nodosa, and ultimately, she responded to treatment with pentoxifylline and topical clobetasol propionate. It is important to be aware of this disease and refer the patient to dermatologists for the appropriate evaluation and treatment.

**Keywords:** Cutaneous polyarteritis nodosa, pentoxifylline, polyarteritis nodosa, Saudi Arabia, topical steroids

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## INTRODUCTION

Cutaneous polyarteritis nodosa (cPAN) is a rare type of cutaneous vasculitis involving the small- and medium-sized arteries of the skin.<sup>[1-3]</sup> cPAN is more commonly reported in adults, and pediatric cases have only sporadically been reported in the literature. The etiopathogenesis of cPAN is not clear. Immune complex is considered to play a role, and several infections such as streptococcus, parvovirus B19, mycobacteria and hepatitis B and C viruses as well as diphtheria–pertussis–tetanus, immunizations, immunodeficiency, inflammatory bowel disease, Behçet’s disease and treatment of acne vulgaris by minocycline have been associated with cPAN.<sup>[1-9]</sup> Recently, a mutation in the gene CERC1, which is associated with a deficiency in the ADA2 protein,

has been implicated in the pathogenesis of cPAN and early-onset vasculopathy.<sup>[10]</sup>

The clinical manifestations of cPAN include tender subcutaneous nodules, livedo reticularis, digital gangrene, cutaneous ulcerations<sup>[1,2,9-12]</sup> and, less commonly, atrophic blanche.<sup>[13]</sup> There may be arthralgia, fever and musculoskeletal pain, especially at the site of skin involvement.<sup>[14]</sup>

It is crucial to differentiate the cutaneous form from the systemic form of polyarteritis nodosa because of the different clinical course and management. The course of cPAN is benign but prolonged, with remissions and relapses, especially the ulcerative lesions.<sup>[1,15-17]</sup>

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There is no well recommended and effective treatment for cPAN. In the milder form, nonsteroidal anti-inflammatory drugs including salicylates have been used, but systemic steroids remained the mainstay of treatment.<sup>[1-3,16-18]</sup> Other drugs that have been used include immunosuppressants such as cyclophosphamide, methotrexate, mycophenolate mofetil pentoxifylline,<sup>[2,18-20]</sup> intravenous immunoglobulins<sup>[21]</sup> other vasodilators,<sup>[22]</sup> biologics<sup>[2]</sup> and topical diflucortolone valerate.<sup>[23]</sup> Penicillin has also been used based on the association of cPAN with streptococcal infection.<sup>[1,2,17]</sup>

In a study by Al Mazyad,<sup>[24]</sup> polyarteritis nodosa was reported in Arab children in Saudi Arabia; however, to the best of our knowledge, the case presented here is the first documented case of cPAN in Saudi Arabia.

## CASE REPORT

A 14-year-old Saudi girl presented to the dermatology clinic at King Fahd Hospital of the University, Al Khobar, Saudi Arabia, with a 2-year history of recurrent multiple lesions on the frontal aspects of the distal lower limbs and pain at the ankle joints. The lesions started as small ulcers and gradually enlarged. There was no history of other skin lesions, fever, Raynaud's phenomena, limb weakness/numbness or other systemic complaints. Family history was irrelevant. The patient had past medical consultations and had been prescribed amoxicillin–clavulanic acid and topical fusidic acid, but without improvement. The skin examination showed multiple ulcerated lesions on the frontal aspects of the ankles and feet [Figures 1 and 2]. Some of the lesions had necrotic bases. Mouth, genital area, hair and nails were normal. The general physical examination and vital signs were normal. The laboratory workup including complete blood count, renal and liver function tests, urine analysis and hepatitis profile were normal or negative. In addition, bone X-ray and computerized tomography scan of the lungs were unremarkable. Erythrocyte sedimentation rate and antistreptolysin O titer were raised, but throat culture was negative. Antinuclear antibody titer was 1:80 of a speckled pattern; however, double-stranded DNA, antineutrophil cytoplasmic antibodies and rheumatoid factors were negative. Neurological, rheumatological and orthopedic consultations showed no abnormality. The biopsy [Figures 3 and 4] showed epidermal changes in the form of acanthosis and focal areas of necrosis in the upper epidermis. The dermis showed widespread perivascular, mostly lymphocytic, infiltrate, with some vessels showing fibrinoid degeneration. Similar vascular changes were seen in the hypodermis, but there was no evidence of panniculitis, the papillary dermis was edematous and the vessels were congested. The patient was treated with

amoxicillin–clavulanic acid and prednisolone, 45 mg daily, and the lesions healed; however, they started to reappear after tapering and discontinuation of prednisolone. Subsequently, the patient was prescribed pentoxifylline, 400 mg/three times daily, and topical clobetasol propionate. The lesions healed [Figures 5 and 6], following which the frequency of pentoxifylline was decreased to once daily and she had remained free of lesions for the past 4 months at the time of reporting this study.

## DISCUSSION

Lindberg<sup>[25]</sup> first described cPAN in 1931 as a cutaneous variant of polyarteritis nodosa without visceral involvement and a more favorable prognosis. The most commonly involved sites are the legs followed by the arms, and the least are the trunk, head and neck.<sup>[1]</sup>

Cutaneous polyarteritis nodosa is not common in children, but it should be considered in a child presenting with vasculitic–necrotic lesions, especially on the distal sites of the limbs. Full workup to exclude systemic involvement is very important. In the presented case, there was no systemic involvement at the time of the presentation and in the subsequent visits for follow-up. To date, only few cases have been reported to have progressed into systemic polyarteritis nodosa.<sup>[26]</sup> The relationship between the cutaneous and systemic form of polyarteritis nodosa has been likened to that of discoid lupus erythematosus and systemic lupus erythematosus, but controversy exists.<sup>[4,11,13,27,28]</sup> Nevertheless, it is advisable to keep patients with cPAN on a close, regular follow-up to check for systemic involvement. As there are no specific serological diagnostic tests, the diagnosis of cPAN is based on histopathology and screening tests for systemic involvement.

Most children have a chronic, relapsing and benign course,<sup>[1-3,16]</sup> as observed in the presented case. Initially, our case responded to corticosteroid but relapsed after its discontinuation, and subsequently, pentoxifylline and topical clobetasol propionate were prescribed. Pentoxifylline, a nonspecific phosphodiesterase inhibitor vasoactive drug with peripheral blood flow improvement and anti-inflammatory activities, and topical diflucortolone valerate have been used individually in the treatment of cPAN with good results.<sup>[23,29]</sup> Thus, as in the presented case, the authors suggest that pentoxifylline with topical steroid can be prescribed to cPAN patients with relapse after discontinuation of systemic steroids.

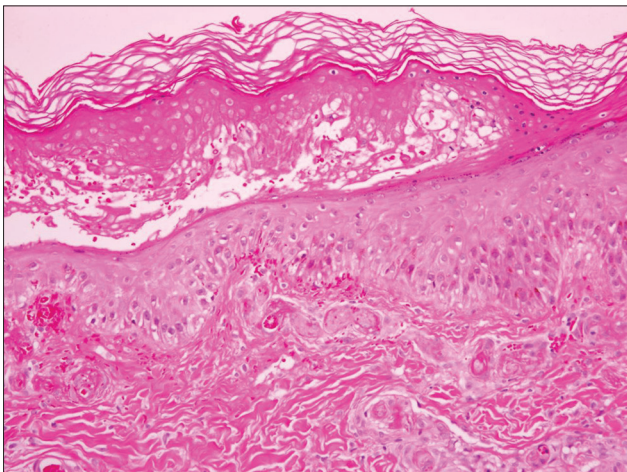
Although cPAN is not a common dermatological disease, it should be considered in the differential diagnosis of multiple



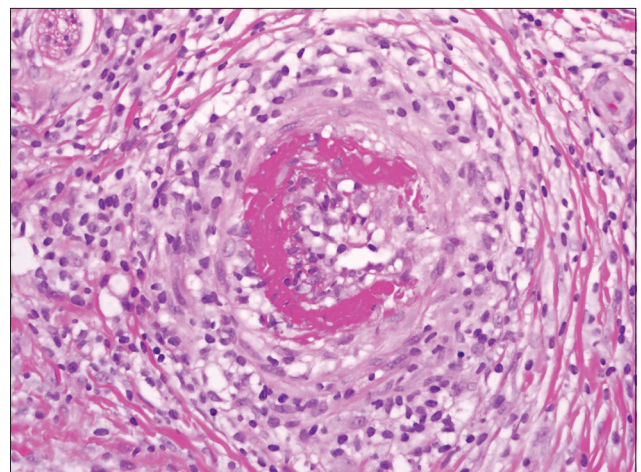
**Figure 1:** Multiple ulcerated lesions on the left ankle



**Figure 2:** Multiple necrotic lesions on the right ankle



**Figure 3:** Necrosis of the upper half of epidermis (hematoxylin and eosin stain)



**Figure 4:** Closer view of the vessel showing fibrinoid necrosis and a predominantly mononuclear perivascular and mural inflammatory infiltrates (hematoxylin and eosin stain)



**Figure 5:** Healed left ankle lesions



**Figure 6:** Healed right ankle lesion

ulceronecrotic lesions on the lower limbs, especially if involving the distal areas, and the patient should be referred to dermatologists for further evaluation and management. In

conclusion, the authors report a case of cPAN successfully treated with oral pentoxifylline and topical steroids.



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**Conflicts of interest**

There are no conflicts of interest.

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