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Cutaneous Polyarteritis Nodosa: A Rare but Severely Debilitating Disease

Alwyn Rapose[1], John Najjar[2]

[1]Division of Infectious Diseases, Assistant Professor of Clinical Medicine, University of Massachusetts, Worcester, MA; [2]Division of Vascular Surgery, Reliant Medical Group, Worcester, Massachusetts. USA 01608.

ABSTRACT

Cutaneous polyarteritis nodosa is a rare cause of ulcerations of the lower extremities. Inflammation and occlusion of small and medium sized cutaneous vessels results in painful nodules and skin ulcerations. Mild cases can be treated with topical corticosteroids or oral nonsteroidal anti-inflammatory medications. Severe cases require corticosteroids and other immunosuppressive therapies. A 47-year-old female patient presented to the infectious diseases outpatient clinic with multiple skin lesions of her lower extremities that failed to respond to courses of oral antibiotics. A deep tissue biopsy confirmed findings of vasculitis and she was initiated on corticosteroids. She developed progressive necrotic lesions as soon as corticosteroids were tapered. Angiography of the lower extremities revealed extensive abnormalities of bilateral tibial arteries and she was advised amputation. The patient sought a second opinion and underwent limb salvage therapy with surgical debridement, skin grafting and hyperbaric oxygen therapy along with systemic corticosteroids. She continues experiencing slow healing and has successfully avoided limb amputations. This case highlights the need to have a high index of suspicion of this rare but highly debilitating form of cutaneous vasculitis. Corticosteroids or other immune-modulating agents along with expert care at a specialized wound center can help patients avoid limb amputation.

Keywords: Cutaneous polyarteritis nodosa, Cellulitis, Tissue Necrosis, Surgical Debridement

***Correspondence to Author:**
Alwyn Rapose, MD, FACP.
Division of Infectious Diseases, Assistant Professor of Clinical Medicine, University of Massachusetts, Worcester, MA.

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Introduction:

Cutaneous polyarteritis nodosa [c-PAN] is a rare form of necrotizing vasculitis most commonly affecting the lower extremities without involvement of internal organs. While the exact etiology remains unknown, it is thought to be caused by an immunologic reaction to a known or unidentified stimulus which causes an inflammation of small and medium sized cutaneous vessels resulting in painful skin nodules and ulcerations. We present a case report of this rare condition in a patient who developed progressive painful necrotic ulcerations of both her lower extremities.

Case Report:

A 47-year-old female presented to the infectious diseases outpatient antibiotic therapy clinic with complaints of severe painful red and black spots on both legs, worsening over the last 5 months. She had previously received several courses of oral antibiotics, a skin biopsy of one of the lesions was non-diagnostic, the biopsy site never healed, and new lesions had started appearing spontaneously. Her past medical history was significant for hypertension, she smoked cigarettes, was not sexually active. She denied fever, chills and other systemic symptoms. Her medications included furosemide, amlodipine, gabapentin and escitalopram none of which were new in relation to the skin lesions. Examination of her legs revealed multiple superficial necrotic lesions bilaterally with surrounding cellulitis and the right shin showed an ulcer with some purulence at the site of previous skin biopsy [Figures 1, 2]. In addition, she had small varicose veins on bilateral ankles. There was no inguinal lymphadenopathy, and the rest of the systemic examination was unremarkable.

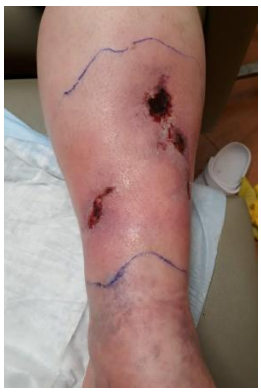


Figure 1: Left leg showing necrotic lesions left leg with cellulitis

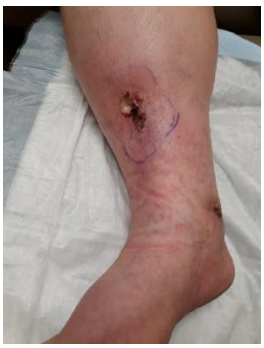


Figure 2: Right leg showing necrotic lesions [including site of biopsy]

The complete blood count revealed mildly elevated white cell count 11.8 x 1000/uL [normal: 3.8 - 10.8 x 1000/uL] with 78 % neutrophils. Hematocrit was normal [38.3%], platelet count was slightly elevated 552 [normal: 140 – 400 x 1000/uL]. She had markedly elevated

inflammatory markers: ESR 120 [normal 2 - 15 mm/h] and CRP 189 [normal < 8.0 mg/L]. Liver enzymes and serum creatinine were normal. She was treated with IV daptomycin 4 mg/kg/day with resolution of the cellulitis in 7 days [Figures 3, 4].

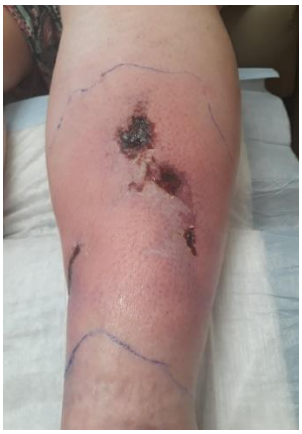


Figure 3: Left leg showing resolution of cellulitis, but progression of tissue necrosis

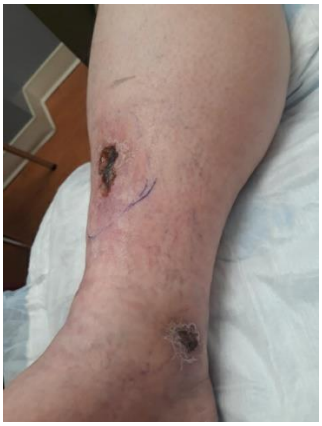


Figure 4: Right leg showing resolution of cellulitis

However, the necrotic painful lesions kept progressing and she underwent a second skin biopsy. The biopsy revealed features of vasculitis including neutrophilic infiltrates surrounding and invading the vessels, fibrinoid necrosis of the vessel wall, nuclear debris and extravasated RBCs. No foci of calcification were found, and special stains were negative for bacteria and fungi. Tissue cultures grew mixed bacteria including *Acinetobacter* species that was sensitive to trimethoprim- sulfametho-xazole. She also underwent CT angiogram of the legs that revealed small atretic appearing bilateral anterior tibial arteries as well as left posterior tibial artery. In addition, she had a short segment high-grade stenosis versus occlusion in the left posterior tibial artery. Differential diagnosis included congenital abnormality versus vasculitis such as polyarteritis nodosa. CT scan imaging of chest, abdomen and pelvis was negative for malignancy. She was tested for HIV, hepatitis B, hepatitis C: the results were negative. Rheumatologic work-up was also negative. Tests included Rheumatoid Factor [RF], ANA, ANCA, anticardiolipin antibody, cryoglobulins, HLA-B27, C3 and C4. A diagnosis of cutaneous polyarteritis nodosa [c-PAN] was established and the patient was started on a tapering course of prednisone along with trimethoprim-sulfamethoxazole. Unfortunately as soon as prednisone was discontinued, the necrotic lesions rapidly progressed [Figures 5, 6, 7].

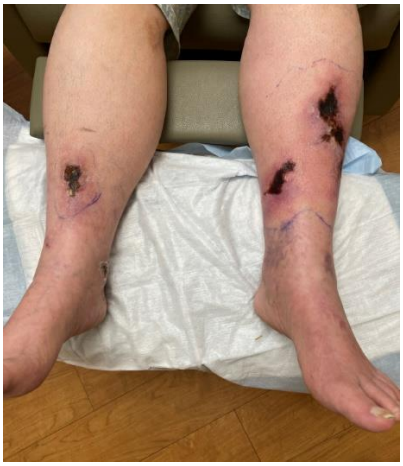


Figure 5: Both legs showing progression of tissue necrosis

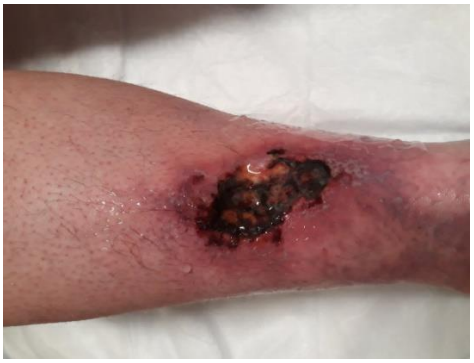


Figure 6: Close-up of left leg showing tissue necrosis

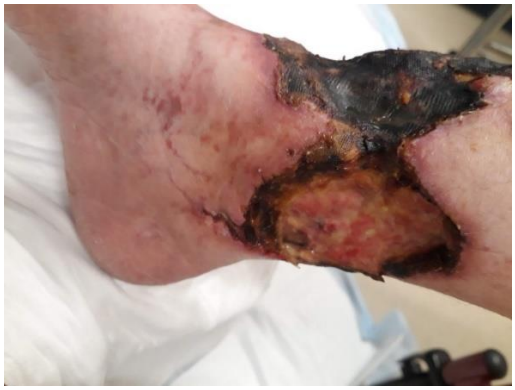
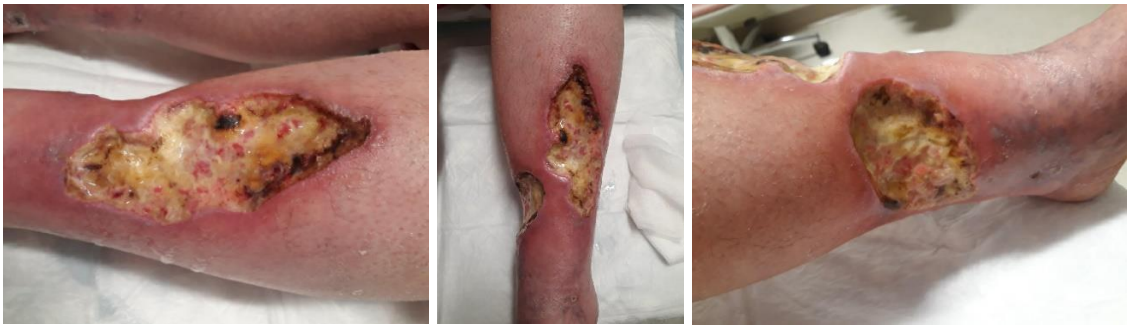


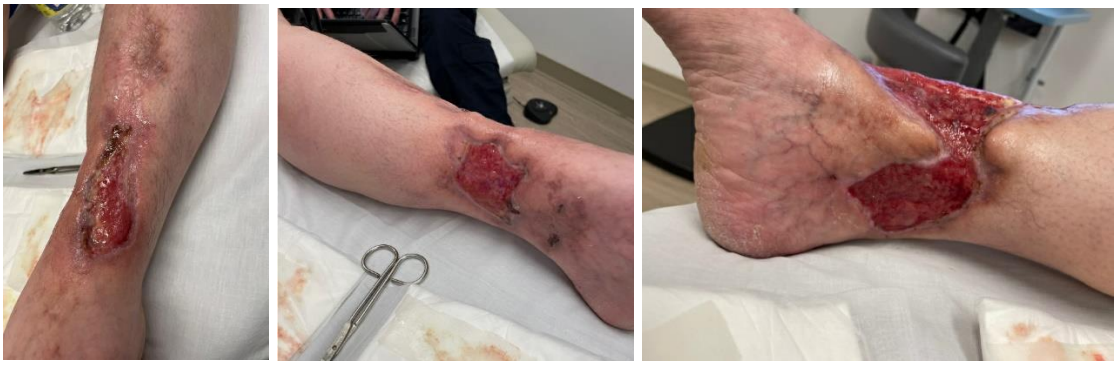
Figure 7: Right leg showing progressive tissue necrosis

A vascular surgery consultation was obtained at another facility. Based on the extensive vessel involvement seen on angiography, the surgery team recommended bilateral lower extremity amputations. The patient declined this recommendation and sought a second opinion. She was evaluated by a second vascular surgery team and underwent extensive surgical debridement on both legs [Figures 8, 9, 10].

Surgical tissue cultures were negative for bacteria. Prednisone was re-initiated. She also underwent aggressive wound care including regular debridement, skin grafting and hyperbaric oxygen therapy [HBOT]. There was a slow but definite response to therapy in the form of gradual healing of the surgical sites with scarring and no appearance of new lesions [Figures 11, 12, 13].



Figures 8, 9, 10: Wound appearance post-surgical debridement



Figures 11, 12, 13: Slow wound healing with scarring

Discussion:

Polyarteritis nodosa [PAN] is a systemic necrotizing vasculitis first described in 1866 by Kussmaul and Maier. The disease predominantly affects medium and small sized vessels in multiple organs, most prominently in the kidneys, heart and liver. This may result in aneurysms, thrombosis, obstruction of blood supply and tissue damage with necrosis in the affected areas. The clinical manifestations vary according to the organ involved and sometimes there is extensive multi-organ involvement resulting in severe disease and death. Omer Karadag and David Jayne published an excellent review on this subject including a historical background to the diagnosis, classification and nomenclature of PAN as well as other related vasculitides [1]. While systemic PAN is often associated with cutaneous involvement, a limited form of this disease called cutaneous polyarteritis nodosa [c-PAN] without involvement of major organ systems exists and was described as early as 1931. [2] Even with this limited form of the disease, there is often significant morbidity due to painful skin nodules, cutaneous ulceration and ischemia [3]. Skin manifestations may be limited or diffuse, but are most often visible in the lower extremities. These include tender subcutaneous nodules which ultimately breakdown leaving painful ulcerations, or lesions present initially as areas of livedo reticularis, which progress to form petechiae, purpura, necrosis and ulceration. The clinical course is characterized by cycles of remissions and recurrences lasting months to several years [3]. Primary c-PAN is idiopathic. Secondary cases may be triggered by a drug, vaccine, or a reaction to infection like streptococcus [4] and hepatitis B virus [HBV] [5]. Other conditions reported to be associated with c-PAN include inflammatory bowel disease, hepatitis C, parvovirus B19, mycobacterium, and medications like minocycline[3]. Multiple other antibiotics as well as non-antibiotic-medications have been implicated in case reports and reviewed extensively by Radic M et al. [6]. Laboratory work-up should include tests like

complete blood count, ESR, CRP [to monitor disease progression and response to therapy], liver and renal function tests, and RF, ANA, ANCA, anticardiolipin antibody, cryoglobulins, HLA-B27, C3 and C4 [to rule out systemic disease]. Confirmation of the diagnosis requires a skin biopsy showing vasculitis i.e. inflammation of the walls of small and medium sized vessels. Histopathology findings depend upon the skin lesion biopsied: Active lesions will show acute inflammatory changes with neutrophilic infiltration of vessel wall, intimal proliferation and thrombosis of the vessel, ulceration and necrosis, older lesions will show fibroblasts and scars. [7, 8] An alternative to skin biopsy is arteriography. Microaneurysms and constrictions of the small and medium sized vessel is the hallmark of PAN [1, 9], but this is more commonly seen in systemic disease [mesenteric and renal vasculature] rather than in limited c-PAN. The treatment of mild cases of c-PAN is with non-steroid anti-inflammatory medications, colchicine, hydroxychloroquin and dapsone. Immunosuppressive agents like corticosteroids [CS] are needed for more severe disease [3, 10]. Alternate steroid-sparing agents like azathioprine, mycophenolate, cyclophosphamide and methotrexate have also been used. HBV-related c-PAN responds well to antiviral therapy. Rarely, patients with c-PAN can progress to systemic disease. [9]

Our patient presented with c-PAN with manifestations limited to her lower extremities. Legs are affected in 95% of cases of c-PAN [4]. Unlike the more commonly reported milder cases of c-PAN, our patient experienced aggressive tissue necrosis requiring extensive debridement resulting in large painful ulcerations. However, with specialized care at a wound center along with HBOT and systemic CS the extensive ulcerations gradually began healing as seen in the clinical photographs. The differential diagnosis of her skin lesions included necrotizing infection, cutaneous vasculitis, pyoderma gangrenosum [PG] and calciphylaxis all of which could present with black necrotic and ulcerative skin lesions. Her initial skin biopsy was non-diagnostic. On review of the biopsy, it was noted to be a shave biopsy and did not include the deeper dermis and subcutaneous tissue. A deep incisional biopsy obtained from a painful nodule or the edge of an ulceration, which includes the subcutaneous tissue is essential to find vasculitis changes in the deeper vessels [3]. This was achieved in the second biopsy. The Von Kossa stain was negative ruling out calciphylaxis, and primary necrotizing skin infection was ruled out by histopathology findings consistent with c-PAN and clinical progression of lesions in spite of appropriately targeted antibiotic therapy. Extensive laboratory work-up as well as radiology failed to find any underlying systemic disease and hence PG was ruled out. Angiography of her lower extremities did reveal findings consistent with c-PAN though classic microaneurysms were not seen. On initial consultation with vascular surgery, based on extensive vessel involvement she was advised bilateral lower extremity amputations. The patient declined this aggressive intervention and preferred conservative debridement of just the necrotic areas. Conservative treatment of her extensive and aggressive disease was challenging because while on one hand CS were required to treat the primary vasculitis, it resulted in delayed wound healing. When CS were tapered, she developed new skin lesions and the dose had to be increased. Also, in-spite of extensive counselling, the patient continued smoking cigarettes and this also contributed to delayed wound healing.

Conclusions:

This case report highlights a number of very important clinical considerations:

1. Cutaneous polyarteritis nodosa is an extremely rare disease and an accurate diagnosis requires a high index of suspicion. A delayed diagnosis can result in progression to extensive ulcerations. The diagnosis can be confirmed by obtaining a deep tissue biopsy and / or imaging studies.

2. Early manifestations are mis-diagnosed as skin infections and patients often received multiple courses of antibiotics as was seen in our patient.
3. An accurate diagnosis can be missed if the skin biopsy performed is superficial.
4. Angiographic findings taken alone can result in aggressive recommendations for amputations as was also seen in our patient.
5. Aggressive c-PAN needs aggressive systemic therapy with high-dose corticosteroids. The necrotic lesions need debridement, and healing can be achieved by optimizing post-debridement wound care along with supplemental therapies like skin grafting and hyperbaric oxygen therapy without the need for amputation.

Authors' contribution: AR: Conception of report + Manuscript draft + Data collection + Review; **JN:** Conception of report + Critical Review

Conflict of Interest: Authors claim no conflict of interest.

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References:

[1]. Karadag O, Jayne DJ. Polyarteritis nodosa revisited: a review of historical approaches, subphenotypes and a research agenda. Clin Exp Rheumatol. 2018 Mar-Apr;36 Suppl 111[2]:135-142.
[2]. Lindberg K. Acta Med Scand 1931; 76: 183-225
[3]. Morgan AJ, Schwartz RA. Cutaneous polyarteritis nodosa: a comprehensive review. Int J Dermatol. 2010 Jul;49[7]:750-6.
[4]. Daoud MS, Hutton KP, Gibson LE. Cutaneous periarteritis nodosa: a clinicopathological study of 79 cases. Br J Dermatol. 1997 May;136 [5]:706-13.
[5]. Minkowitz G, Smoller BR, McNutt NS. Arch Dermatol 1991 Oct;127[10]:1520-3. Benign cutaneous polyarteritis nodosa. Relationship to systemic polyarteritis nodosa and to hepatitis B infection.
[6]. Radić M, Martinović Kaliterna D, Radić J. Drug-induced vasculitis: a clinical and pathological review. Neth J Med. 2012 Jan;70[1]:12-7.
[7]. Chen K R. J Dermatol. 1989 Dec;16[6]:429-42. Cutaneous polyarteritis nodosa: a clinical and histopathological study of 20 cases.
[8]. Bauzá A, España A, Idoate M.Cutaneous polyarteritis nodosa. Br J Dermatol. 2002 Apr; 146[4]:694-9.
[9]. De Virgilio A, Greco A, Magliulo G, et al. Polyarteritis nodosa: A contemporary overview. Autoimmun Rev. 2016 Jun;15 [6]:564-70.
[10]. Hočevar A, Tomšič M, Perdan Pirkmajer K. Clinical Approach to Diagnosis and Therapy of Polyarteritis Nodosa. Curr Rheumatol Rep. 2021 Feb 10; 23[3]:14.