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INVITED REVIEWS

Cutaneous arteritis: Description based on Chapel Hill Conference Consensus 2012 and a case report

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Definition

According to the overview of the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides (CHCCNV), cutaneous polyarteritis nodosa (cPAN) has been reclassified as cutaneous arteritis (CA), a form of single-organ vasculitis [1]. Single-organ vasculitis refers to vasculitis that exclusively affects one organ and lacks systemic involvement. CA specifically targets the skin and is characterized by involvement of small to medium-sized blood vessels [2]. Clinical manifestations encompass subcutaneous nodules, livedo reticularis, ulcers, and purpura. This chronic, recurring vasculitis primarily affects the small arteries and arterioles at the panniculus and the dermal-subcutaneous junction. Diagnosis relies on recognizing typical skin lesions, the absence of systemic symptoms, and corroborative histopathological findings [3].

Etiology

CA is a rare disease, and the true incidence is unknown. This cutaneous vasculitis affects patients of all ages, and there is no gender predominance.

The cause of CA remains uncertain. It might emerge from an underlying condition, infections (such as group A β hemolytic streptococcus, hepatitis B, hepatitis C, parvovirus B-19, and mycobacterium tuberculosis), or drug usage (notably, minocycline-induced cPAN has been well-documented) in around 10-15% of instances. Additionally, malignancies contribute to the vasculitis's onset in 5% of cases, involving both hematologic and solid organ malignancies [2,4].

Connective tissue diseases (systemic lupus erythematosus, rheumatoid arthritis, sjögren syndrome) and inflammatory diseases (inflammatory bowel diseases, cryoglobulinemia type 2 and 3, antineutrophilic cytoplasmic antibody (ANCA)-related vasculitis and Behçet's disease) are the etiologic factors in 15–20% of the cases. An association between cPAN and inflammatory bowel disease has been established in a case series. Among 79 patients diagnosed with cPAN, 5 cases were also diagnosed with inflammatory bowel disease (comprising four cases of Crohn's disease and one case of ulcerative colitis) [5,6].

Clinical Features

CA typically manifests initially as livedo reticularis (in 56% of cases), along with tender subcutaneous nodules or skin ulcerations. Additional observed symptoms encompass purpura, cutaneous necrosis, and localized extracutaneous manifestations. The condition primarily affects the legs, followed by the arms and trunk [4].

It usually has a benign course but usually, relapses occur, especially in patients with ulcers and increased acute phase reactants. Extra-cutaneous manifestations of CA include constitutional symptoms such as myalgias, arthralgias, and neuropathy, but these are not the evidence of a systemic disease [5].

Diagnosis

The current diagnostic criteria for cPAN were proposed in 2009 by Nakamura et al., and include the presence of cutaneous manifestations and histopathological findings without systemic involvement [3]. The diagnosis is based on typical lesions in a deep incisional cutaneous biopsy, as there are no specific serological tests. Direct immunofluorescence (DIF) frequently reveals the presence of IgM and C3 deposits within the affected arterial walls, indicating its association with immune complex-mediated pathology.

Treatment

Treatment choice dependes on the severity of skin lesions. Non-steroidal anti-inflammatory drugs and colchicine may be preferred in mild to moderate cases. In cases that prove refractory and involve severe pain, ulcers, or necrosis, treatment options often include prednisolone (30-60 mg/day), hydroxychloroquine, dapsone, azathioprine, cyclophosphamide, methotrexate, mycophenolate mofetil, sulfapyridine, pentoxyphylline, and intravenous immunoglobulin. It is important to note that there is no treatment with established efficacy through prospective trials [7].

Differential diagnosis

CA must be distinguished from systemic (PAN) sPAN is characterized by identical cutaneous findings and the presence of systemic organ involvement including liver, kidney, and heart. The extra-cutaneous manifestations of peripheral neuropathy and myalgia in CA can occur only in adjacent to the cutaneous lesions, while they may be disparate in systemic PAN [3].

Furthermore, it's crucial to differentiate from other forms of vasculitides, such as microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), eosinophilic granulomatous polyangiitis (EGPA), erythema induratum, and urticarial vasculitis (Table 2) [5]. GPA and EGPA also affect small- to medium-sized vessels. Pulmonary involvement, granulomatous inflammation, and anti-neutrophil cytoplasmic antibody (ANCA) positivity are common in both. MPA typically affects small vessels, in the kidneys and lungs. Urticarial vasculitis is also a small-vessel vasculitis demonstrated with painful burning urticaria (lasting longer than 24 hours) and arthralgias, which do not occur in CA.

CASE REPORT

A twenty-one-year-old woman presented with a complaint of painful subcutaneous erythematous nodules on both her upper and lower extremities, persisting for a duration of five months. There was no history of purpura, Raynaud's phenomenon, recurrent oral ulcers, hair loss, or malar rash. On physical examination, she had multiple

Table 1. A new draft of diagnostic criteria for cutaneous polyarteritis nodosa [3]

1. Cutaneous manifestations
Subcutaneous nodules, Livedo, Purpura, Ulcers
2. Histopathological findings
Fibrinoid necrotizing vasculitis of small and medium-sized arteries
3. Exclusion manifestations
(1) Fever (=38°C, =2 weeks), Weight loss (6 kg or more in 6 months)
(2) Hypertension
(3) Rapidly progressive renal failure, Renal infarction
(4) Cerebral hemorrhage, Cerebral infarction
(5) Myocardial infarction, Ischemic heart disease, Pericarditis, Heart failure
(6) Pleuritis
(7) Intestinal hemorrhage, intestinal infarction
(8) Peripheral neuropathy out of the affected skin lesion
(9) Arthralgia (arthritis) or myalgia (myositis) out of the skin lesion
(10) Abnormal arteriography (multiple microaneurysms, stenosis, and obliteration)
4. Decision
Both cutaneous manifestations and histopathological findings without exclusion manifestations

Table 2. Differential diagnosis and questioning of cutaneous vasculitis [5]

Systemic polyarteritis nodosa	Medium-sized arterial vasculitis, punched out ulcers, hypertension, renal failure, hematuria, abdominal pain, and microaneurysms on MRI
Microscopic polyangiitis	Small and medium-sized vessel vasculitis, involving the kidneys and lungs. Palpable purpura, constitutional symptoms, glomerulonephritis, alveolar hemorrhage, and p-ANCA>c-ANCA
Eosinophilic granulomatosis with polyangiitis	Granulomatous vasculitis, asthma, allergic rhinitis, palpable purpura, subcutaneous nodules, peripheral eosinophilia, and p-ANCA
Granulomatosis with polyangiitis	Necrotizing granulomatous small vessel vasculitis, cutaneous and oral ulcerations, upper and lower respiratory tract involvement, glomerulonephritis and c-ANCA
Livedoid vasculopathy	Superficial dermal vasculopathy, atrophie blanche with peripheral telangiectasia and punched out ulcers on ankles
Erythema induratum	Lobular or mixed panniculitis small or medium-sized vessel vasculitis, erythematous nodules and plaques that may ulcerate on dorsal legs
Urticarial vasculitis	Leukocytoclastic vasculitis, and urticaria lasting >24 hours.

subcutaneous ulcers predominantly distributed over all extremities. Laboratory tests including complete blood count, liver and kidney function tests, and serum complement levels were within normal ranges. Anti-nuclear antibody (ANA), ANCA, and rheumatoid factor (RF) were negative. Histopathologic examination of the subcutaneous nodule revealed neutrophilic vasculitis of the dermal medium and small vessels (Figure 1).

The patient was treated with methylprednisolone of 20 mg/day and colchicine of 1 mg/day. Methylprednisolone was tapered and discontinued in the 3rd month. The lesions completely resolved over a period of three months and the patient was on regular follow-up. Colchicine treatment was discontinued after 2 years and then she was in remission. There was no new lesion at the last control (in the 4th year of the disease) 1 month ago.

Key messages

- Cutaneous arteritis (previously known as cutaneous polyarteritis nodosa) is an uncommon form of single-organ vasculitis that targets the deep skin vessels and subcutaneous tissue
- This condition tends to be chronic and benign, occasionally exhibiting a relapsing pattern.
- Diagnosis relies on recognizing the characteristic clinical and histopathological traits.
- The seriousness of the skin manifestations determines treatment approaches; however, it's important to note that there is no treatment with proven efficacy based on prospective trials.

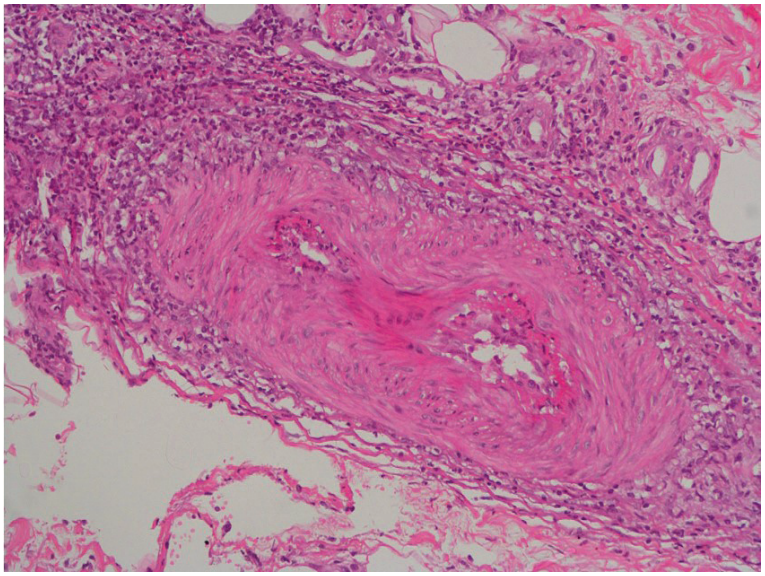

Figure 1. Mild fibrinoid necrosis with moderate vessel wall thickening and inflammatory infiltrate of lymphocytes and neutrophils advancing to the vessel wall.

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