

# Cutaneous Polyarteritis Nodosa Associated with Destructive Arthritis

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**C**utaneous polyarteritis nodosa (CPAN) is a rare form of vasculitis characterized by a necrotizing inflammation of the small- to medium-sized muscular arteries located in the deep dermis and subcutis [1]. The disease is distinguished from polyarteritis nodosa (PAN) by the lack of major visceral symptoms. Unlike PAN, CPAN has a benign prolonged or episodic course with periodic exacerbations and spontaneous or treatment-induced remissions. There is no major systemic involvement, but the hundreds of cases reported in the literature to

date have shown that the cutaneous manifestations may be accompanied by mild signs and symptoms such as fever, myalgia, arthralgia, and peripheral neuropathy [2]. Although arthralgia occurs with high frequency, the documented cases of arthritis, particularly destructive arthritis, are very rare. In this report we describe a patient with CPAN and destructive arthritis.

## PATIENT DESCRIPTION

A 66 year old Caucasian woman presented to the dermatology department of a tertiary medical center with livedoid eruption involving the lower limbs of 8 years duration. In the preceding 3 years she had experienced two episodes of left dorsal foot ulcers that resolved with local treatment. Past medical history was remarkable for foot numbness of 3 years duration and

erosive arthritis in the left ankle and mid-foot lasting 12 years. Additional diagnoses included benign essential hypertension, hyperlipidemia and gastritis.

Physical examination revealed normal vital signs, systolic heart murmur and bilateral ankle edema with left ankle tenderness and limited range of motion due to pain. On skin examination, patchy reticulated violaceous macules involving both shins and ankles were noted [Figure 1A] as well as small erythematous and skin-colored nodules on the ankles and dorsal feet [Figure 1B]. The nodules were slightly tender. Excisional skin biopsy specimen from a nodule showed histopathological findings consistent with PAN: a medium-sized artery between the reticular dermis and subcutis, with fibrinoid necrosis of the intima and neutrophil infiltration within and around the arterial wall, which was



**Figure 1.** [A] Livedo reticularis involving the lower limbs. [B] Small erythematous and skin-colored nodules on the ankles and dorsal feet. [C] Computed tomography of the feet demonstrating extensive erosive changes in the left midfoot (arrows) and the subtalar joint (arrowhead)

largely destroyed. A biopsy specimen from another nodule demonstrated a small-sized artery in the reticular dermis with lymphocytic infiltrate within the arterial wall and thrombus within the lumen. Elastic tissue stain disclosed elastic remnants in the affected arterial wall.

At presentation, laboratory workup was remarkable for elevated erythrocyte sedimentation rate (60 mm/hour) and positive antinuclear antibody (ANA) (1:160, by immunofluorescence). Findings were normal or negative for the following relevant laboratory analysis: complete blood count, serum creatinine, uric acid, liver enzymes, urinalysis, complement level, anti-double stranded DNA (dsDNA), anti-Smith (Sm), anti-Ro/SS-A, anti-La/SS-B, anti-ribonucleoprotein (RNP), rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), anti-proteinase-3 and myeloperoxidase, anticardiolipin and  $\beta$ 2 glycoprotein, lupus anticoagulant, protein S, protein C, cryofibrinogen, cryoglobulins, anti-streptolysin-O, serology for hepatitis B and C, tuberculin test, and fecal blood test. Of note, ANA had been negative 12 years earlier. Relevant laboratory analysis for arthritis evaluation was normal when arthritis was first diagnosed.

Transthoracic echocardiography demonstrated a mild left ventricular hypertrophy with normal systolic function and no valvular abnormality. Nerve conduction study revealed bilateral axonal neuropathy of the lower limbs. On computed tomography (CT) of the feet, extensive erosive changes were observed in the left mid-foot and ankle joints [Figure 1C]; findings on CT of the hands were unremarkable. Magnetic resonance imaging of the left foot and ankle revealed the same erosive changes in addition to tenosynovitis of the flexor and peroneal tendons.

On the basis of the cutaneous findings and histopathologic features, together with the absence of any visceral signs of PAN except for peripheral neuropathy and destructive arthritis that were confined to the area of the skin lesions, the patient was diagnosed with CPAN. Treatment consisted of a combination of prednisone 40 mg/

day and methotrexate up to 20 mg/week. Several weeks later, the subcutaneous nodules disappeared and the signs of arthritis completely resolved. However, there was no amelioration of the livedo reticularis or foot numbness. The prednisone dosage was decreased gradually as was methotrexate dosage and for the last 31 months the patient has been receiving treatment with methotrexate only (10 mg/week). During 39 months of follow-up under treatment there was no relapse.

### COMMENT

CPAN affects small- to medium-sized arteries located within the reticular dermis and/or subcutis. The most common site of involvement is the lower limbs. Small tender subcutaneous nodules, sometimes ulcerative, and livedo reticularis are typical clinical findings [2]. Less frequently, purpura, digit infarcts, and atrophic blanche are noted [2]. Histopathologic study reveals segmental pan-arteritis. Recently, Nakamura et al. [3] suggested that diagnostic criteria for CPAN include both the cutaneous manifestations and the histopathologic findings, together with exclusion of systemic manifestations, such as fever ( $\geq 38^{\circ}\text{C}$  for  $\geq 2$  weeks), weight loss ( $\geq 6$  kg in 6 months), hypertension, rapidly progressive renal failure and renal infarction, cerebral hemorrhage or infarction, myocardial infarction, heart failure or pericarditis, intestinal hemorrhage or infarction, and abnormal arteriography. Additional exclusion criteria are peripheral neuropathy, myalgia, and arthralgia or arthritis that are not confined to the area of cutaneous involvement.

Arthralgia in the area of cutaneous involvement is thought to be relatively common in CPAN [3], although arthritis, specifically destructive arthritis, is extremely rare. To the best of our knowledge, only five cases of CPAN complicated by destructive arthritis have been reported previously [4]. In our case, the seronegative localized destructive arthritis, together with normal serum uric acid levels and absence of other joint involvement or psoriasis,

did not support the presence of an erosive arthritis such as rheumatoid arthritis, psoriatic arthritis, or tophaceous gout.

Another possible etiology was indolent infection due to *Mycobacteria* for example, but tuberculin test was negative, and a biopsy obtained from the left ankle synovium 10 years before admission had not revealed granuloma or any infectious agent. Therefore, CPAN-associated destructive arthritis was diagnosed. As in our patient, two of the patients reported in the literature had also acquired arthralgia before the appearance of the cutaneous signs and symptoms.

Until today, only one study has documented progression of CPAN to systemic PAN, in 2 of 20 patients after 18 and 19 years [5]. In our patient systemic involvement has not been detected after a follow-up of 15 years, similar to the five previously reported cases of CPAN with destructive arthritis. Therefore, we assume that the destructive arthritis in our patient does not herald progression to systemic PAN, although longer follow-up is needed to reach a definitive conclusion.

In summary, we suggest that destructive arthritis confined to the area of skin involvement be added to the possible systemic signs of CPAN.

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