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Cutaneous Polyarteritis Nodosa: Uncommon and Rare Form of Cutaneous Vasculitis

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Abstract

Cutaneous polyarteritis nodosa (CPAN) is a variant of polyarteritis nodosa that is limited primarily to the skin. It is a chronic recurrent disorder characterized by the presence of nodular lesions with or without ulceration on the distal third of the lower limbs. Nodular vasculitis and thrombophlebitis can be clinically or pathologically mistaken for CPAN. We present a case of a 51-year-old woman with painful nodules on the lower limbs. Some of the nodules were ulcerated. Histopathological examination of a nodule on deep incisional biopsy revealed fibrinoid necrosis of a medium-sized artery in the subcutis along with perivascular mixed infiltrate. The patient did not have any symptoms or signs of internal organ involvement. The possible etiological factor has not been detected. The patient was treated with oral prednisone 0.5 mg/kg/day and dapson 150 mg/day. Over the one-year follow-up the lesions showed regression, with one minimal relapse which resolved after the short course of oral prednisone.

Key words: Polyarteritis Nodosa; Skin Diseases; Chronic Pain; Prednisone; Biopsy; Treatment Outcome

Introduction

Cutaneous polyarteritis nodosa (CPAN) is a chronic, recurrent vasculitis that affects small arteries and arterioles in the panniculus and the dermal-subcutaneous junction (1). It still remains controversial whether CPAN is a skin symptom of polyarteritis nodosa (PAN), or a distinct clinical entity with different pathogenesis (2). The common clinical features of CPAN are multiple subcutaneous nodules or livedo and macules, with or without ulceration, affecting the lower extremities. Other symptoms may be associated with CPAN, such as constitutional, neurological, and musculoskeletal ones, limited to the affected areas (1, 3). Nodular vasculitis and thrombophlebitis can be clinically or pathologically mistaken for CPAN (4). The diagnosis is based on skin biopsy, as there are no specific serological tests (5).

Case Report

A 51-year-old woman presented with the erythematous, painful nodules on the lower limbs lasting for 7 months. The lesions were first diagnosed and treated as vasculitis nodularis with no improvement. On admission in our Clinic, physical examination showed asymmetrical, tender painful nodules and irregular ulcerated subcutaneous nodules over both legs (Figures 1 and 2). Routine investigations, including erythrocyte sedimentation rate, C-reactive protein, complete blood count with differential, blood levels of electrolytes and glucose, liver and renal function tests and urinalysis were normal. Antinuclear antibodies, anti-neutrophil cytoplasmic antibodies and anti-streptolysin-O were normal or negative. Serology tests for hepatitis B, C and HIV 1/2 were negative. QuantiFERON-TB Gold test was negative. Chest X-ray, echocardiography of the heart and ultrasonography of the abdomen showed no pathologic findings. The patient did not have any symptoms or signs of internal organ involvement. Deep incisional skin biopsy of the nodulus revealed fibrinoid necrosis of small arteries in the subcutis along with perivascular mixed infiltrate (Figures 3 and 4). The patient was treated with oral prednisone 0.5 mg/kg/day and dapson 150 mg/

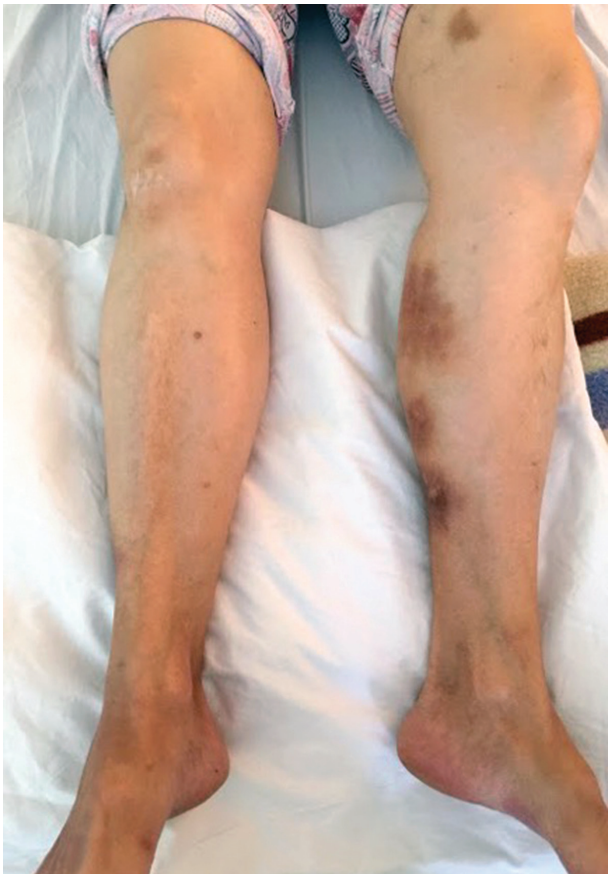

Figure 1. Reddish-purple nodules on the lower extremities

day. After 2 months, the lesions showed regression with residual hyperpigmentation and scarring and the dose of prednisone was then slowly decreased and discontinued. In further 10 months the patient experienced one minor relapse, therefore she received another course of prednisone for several weeks. On the last check-up, 12 months after the hospitalization, the patient was free of active lesions.

Discussion

CPAN was initially described in 1931 by Lindberg as the case of necrotizing vasculitis, which was limited to the skin but could not have been histopathologically distinguished from systemic PAN (6). CPAN more frequently affects women (male: female ratio = 1:1.7), aged ≥ 40 years, with numbers of patients peaking at 50–59 years of age (7). The lesions commonly occur on the legs in 97%, followed by the arms in 33%, and the trunk in 8% of patients. Additional involvement of the head and neck has been noted in 9 of 23 patients (39%) with CPAN (3). The skin manifestations of CPAN include subcutaneous nodules (80-100%), livedo reticularis (45-80%), ulcers, and gangrene. Other findings include purpura, papules, atrophie blanche, and leg edema. The nodules frequently have a diameter of 5-15 mm and are multiple, red-dark to reddish-purple, and are accompanied by spontaneous pain and tenderness. These nodules, with or without livedo reticularis, are usually the first presentation of the disease, and are the predecessor to ulceration in 50-59% of

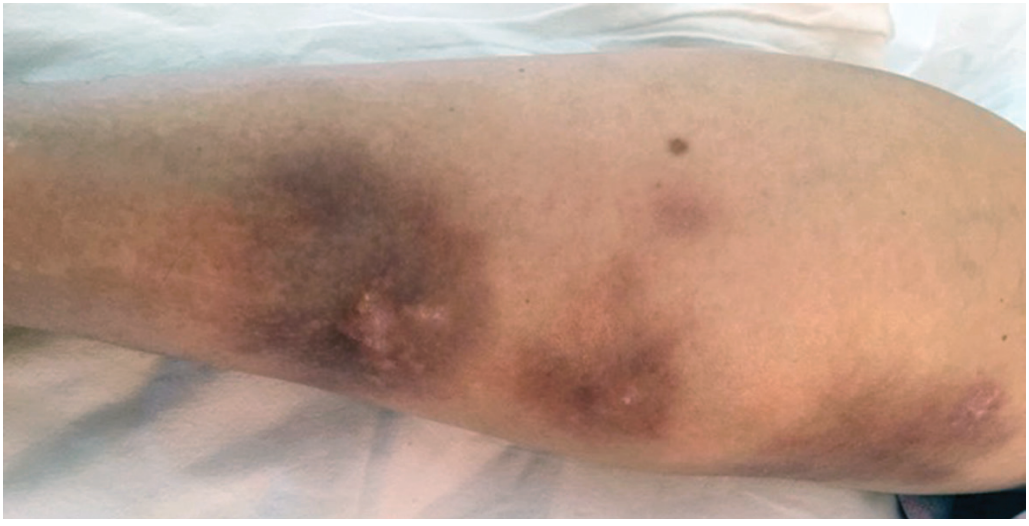

Figure 2. Erythematous nodule with a central crust on the left leg

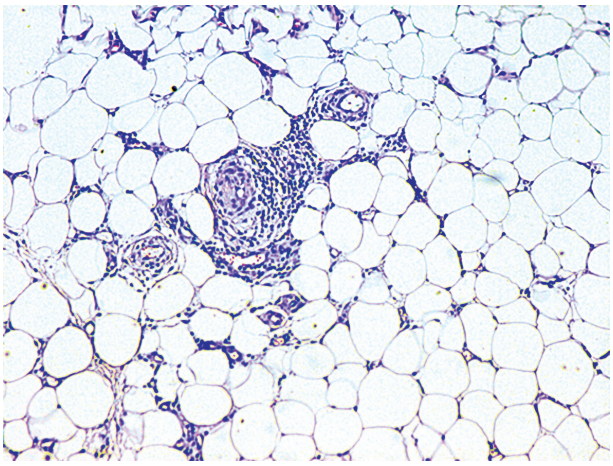

Figure 3. Fibrinoid degeneration of the vessel wall with perivascular mixed infiltrate of lymphocytes, histiocytes and a few neutrophils into the subcutis (haematoxylin-eosin stain ×100)

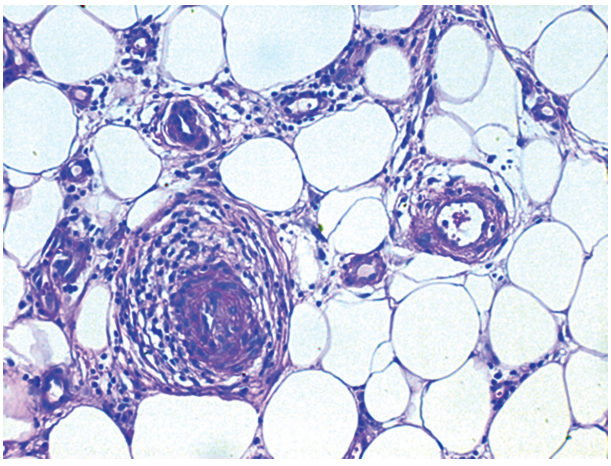

Figure 4. Fibrinoid degeneration, intimal proliferation and an almost complete obliteration of the vessel wall lumen (Periodic acid-Schiff stain ×200)

the cases (2, 7, 8). Extra-cutaneous manifestations of CPAN include constitutional symptoms, fever, myalgias, arthralgias, and peripheral neuropathy (mononeuropathy and mononeuritis multiplex) (3). In the patients with an ulcerated CPAN, a more chronic course of the disorder with neurological involvement is common (8). Unlike the systemic disease, CPAN does not show immunologic abnormalities (9). Absence of the life-threatening organ involvement in CPAN (renal ischemia, testicular pain/epididymitis, ischemic myalgia and hypertension) distinguishes CPAN from the systemic PAN (10). Our patient did not have any symptoms or signs of the internal organ involvement.

The diagnosis of CPAN is based on clinical features of isolated skin involvement confirmed by histopathological findings (5). Deep, surgical incisional biopsies are essential for the correct diagnosis of CPAN. A punch biopsy is not recommended, because it often fails to sample larger vessels that are typically affected (4). Serial sections may also be necessary to demonstrate the vasculitis, particularly when the involvement is segmental and focal (9). The microscopic findings of CPAN can be divided into four stages: (1) degenerative stage with degeneration of arterial wall and deposition of fibrinoid material and partial or complete destruction of internal and external elastic laminae; (2) acute inflammatory stage with an infiltrate mostly composed of neutrophils with some eosinophils around and within the arterial wall; (3) granulation tissue stage with an infiltrate also containing lymphocytes and macrophages and intimal proliferation and thrombosis with occlusion of the lumen leading to ulceration; and (4) healed end-stage with fibroblastic proliferation extending in the perivascular area (4, 11).

Nodular vasculitis is a lobular panniculitis and vasculitis affecting mostly venules or septal veins and less commonly arteries. In contrast, CPAN is an arterial vasculitis with minimal extension of its inflammation into the adjacent subcutis. The pattern of elastic tissue distribution and vessel silhouette is a diagnostic aid to differentiate between venous and arterial vasculitis (4). Superficial thrombophlebitis is a sequela of degenerative or anatomical alterations of vessel walls in lower legs, slowed blood flow, and/or hypercoagulable conditions, which then secondarily lead to inflammatory infiltration (1). Two other entities have recently been described, macular arteritis and lymphocytic thrombophilic arteritis that show clinical features of CPAN but a lymphocytic arteritis on biopsy (12, 13). These variants of vasculitis may simply represent latent or late evolutionary stages of CPAN (4). The etiology of CPAN is unknown. Associations with various viral (particularly HBV as well as HCV, HIV 1/2 and parvovirus B19) and group A streptococcal infections have been reported (2). Minocycline-induced CPAN is a well documented

phenomenon (14). In our patient, a possible etiological factor has not been detected.

Systemic corticosteroids remain the mainstay of treatment for CPAN and most patients seem to respond to oral prednisone. Successful treatment outcomes were reported with dapsone, colchicines, azathioprine, methotrexate, cyclosporine, cyclophosphamide, NSAIDs, sulphapyridine, pentoxyphylline, and intravenous immunoglobulin. Antibiotic treatment may be needed in patients with documented streptococcal or other bacterial infections (2, 3). The prognosis of CPAN is favorable with no known mortality from the disease itself. The course is chronic with relapses and remissions that may occur spontaneously or following treatment (5). However, since progression to systemic PAN may occur in some patients, careful follow-up is necessary (7).

In summary, CPAN is a rare and benign cutaneous vasculitis of unknown etiology and can be challenging to diagnose and manage. There are no specific clinical and laboratory findings. The diagnosis is based on clinical features of isolated skin involvement confirmed by histopathological findings. Systemic corticosteroids and dapson are effective in the treatment of CPAN. Long-term follow-up is necessary for CPAN because it can progress to systemic PAN.

Abbreviations

CPAN – cutaneous polyarteritis nodosa
PAN – polyarteritis nodosa

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Kutani poliarteritis nodoza: neobičan i redak oblik kutanog vaskulitisa

Sažetak

Kutani poliarteritis nodoza predstavlja varijantu nodoznog poliarteritisa koja je ograničena samo na kožu. Kutani poliarteritis nodoza ima hronični, rekurentni tok i klinički se manifestuje u vidu nodusa sa ulceracijom ili bez nje, lokalizovanih na distalnim trećinama donjih ekstremiteta. U praksi se često klinički i histopatološki dijagnostikuje kao vaskulitis nodularis ili tromboflebitis. Prikazujemo pacijentkinju uzrasta 51 godinu sa bolnim nodusima na donjim ekstremitetima, od kojih su pojedini bili egzulcerisani. Histopatološki nalaz duboke incizione biopsije nodusa pokazao je fibrinoidnu nekrozu arterija srednjeg kalibra u supkutisu i mešoviti

perivaskulni infiltrat. Pacijentkinja nije imala nijedan simptom ni znak sistemskog vaskulitisa. Mogući etiološki faktor nije detektovan. Pacijentkinja je lečena prednizonom 0,5 mg/kg/dan i dapsonom 150 mg/dan. Došlo je do regresije promena tokom narednih godinu dana, uz jedan minimalan recidiv nakon nekoliko meseci koji je rešen kratkotrajnom primenom prednizona.

Ključne reči: Poliarteritis nodoza; Kožne bolesti; Hronični bol; Prednizon; Biopsija; Ishod terapije

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