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Case Report

Cutaneous polyarteritis nodosa: a form of benign vasculitis

皮膚結節性動脈外層炎：一種較溫和的血管炎

LS Ku 顧立誠

A 37-year-old hepatitis B male carrier presented with painful nodules over both lower limbs for 10 years. Medium sized vasculitis was confirmed by skin biopsy. Features of peripheral neuropathy, cryoglobulinaemia, elevated anti-cardiolipin IgM and hypocomplementaemia were demonstrated. He responded well to non-steroidal anti-inflammatory agents and systemic involvement was not found.

一位三十七歲男性乙型肝炎帶菌者主訴雙下肢痛性結節達十年。皮膚活檢確診為結節性動脈外層炎。臨床表現包括週圍神經病，冷凝球蛋白血症，M型抗心肌磷脂免疫球蛋白升高及低補體血症。此患者對非固醇類抗炎藥治療反應良好，並無累及其他系統器官。

Keywords: Cutaneous polyarteritis nodosa

關鍵詞：皮膚結節性動脈外層炎

Introduction

Cutaneous polyarteritis nodosa (CPN) is a rare cutaneous vasculitis that affects the medium to small muscular arteries of the skin. It carries a good prognosis and runs a prolonged course with relapse and remission. Conservative therapeutic plans should be adopted.

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Case report

A 37-year-old Chinese hepatitis B male carrier presented with a ten year history of painful inflammed linear cords and nodules over both lower limbs. The left lower limb was more severely affected than the right side and other parts of the body were spared. The lesions were fleeting, developed and resolved spontaneously with post-inflammatory hyperpigmentation. There was cyanotic discoloration over both lower limbs on cold exposure but there was no definite history suggestive of Raynaud's phenomenon. Paresthesia over the left heel and left ankle was felt. There was no history of transient ischaemic attack, stroke, deep vein thrombosis, persistent myalgia,

arthralgia, abdominal pain or gastrointestinal bleeding. He was suffering from diabetes mellitus on oral hypoglycaemic agents. His family history was unremarkable.

General examination was normal and his blood pressure was 110/70 mmHg. Actively inflammed tender subcutaneous nodules and linear cord-like swellings were noted over both lower limbs (Figure 1). Livedo reticularis and multiple linear post-inflammatory hyper-pigmentation were evident (Figure 2). There was decreased pin-prick sensation over the left heel and left ankle but the distribution did not conform to any dermatome. There was no ulceration, no atrophie blanche and all distal arterial pulses of the lower limbs were present. No foot drop, nerve palsy or other neurological deficit was noted. The clinical differential diagnoses include superficial migratory thrombophlebitis, polyarteritis nodosa, livedo vasculopathy, and panniculitis such as erythema nodosum.

Investigations including the complete blood counts, liver and renal function tests were normal except that alkaline phosphatase was slightly raised to 130 U/L (47-113 U/L). C3 was decreased to 0.66 g/L (0.74-1.44 g/L) while C4 was normal. Immune markers including antinuclear factor, anti-DNA, extractable nuclear antigen antibody, antineutrophil cytoplasmic antibody were all negative. Clotting profile, immunoglobulin pattern, serum protein electrophoresis were normal. Anticardiolipin IgM was elevated at 21 MPL/ml (<13 MPL/ml) while the anticardiolipin IgG level was normal. Hepatits B surface antigen and serum cryoglobulin were positive and anti-hepatitis C virus antibody was negative. Urinalysis showed glycosuria. Anti-streptolysin O titre, VDRL, erythrocyte sedimentation rate (ESR), rheumatoid factor, alpha fetal protein were all normal. Stool for occult blood was negative. Deep incisional biopsy on the left knee for histopathology and immunofluoresecent study showed basketweave cornified layers with relatively intact epidermis. A

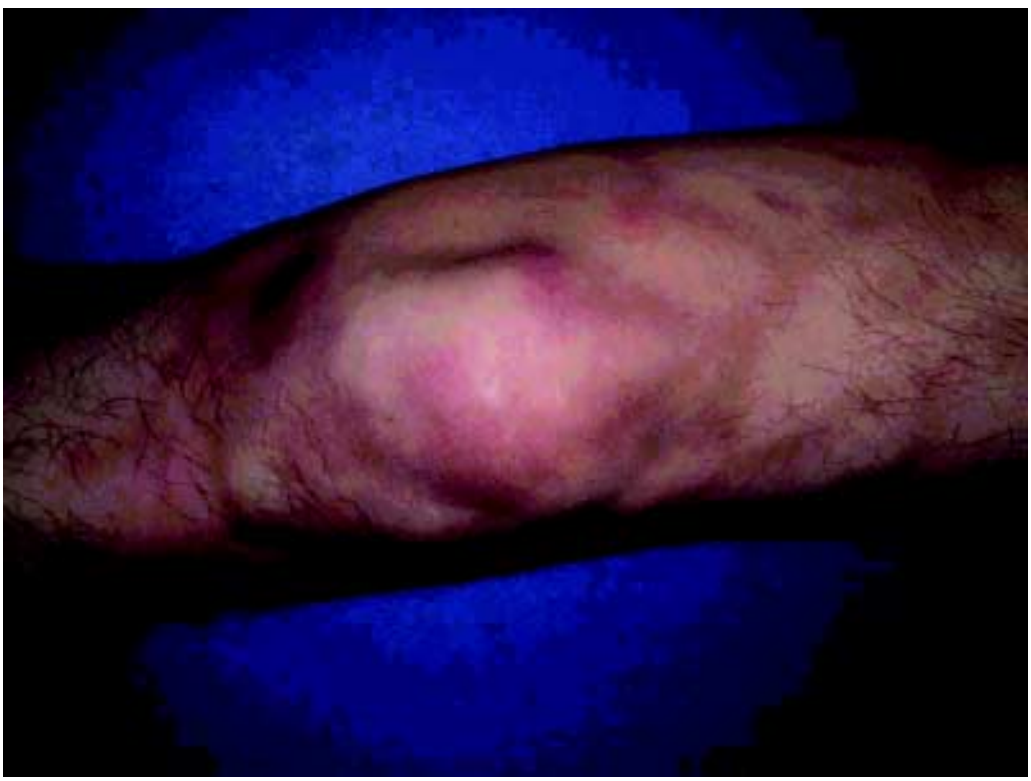

Figure 1. Actively inflamed tender subcutaneous cords and nodules over left knee.

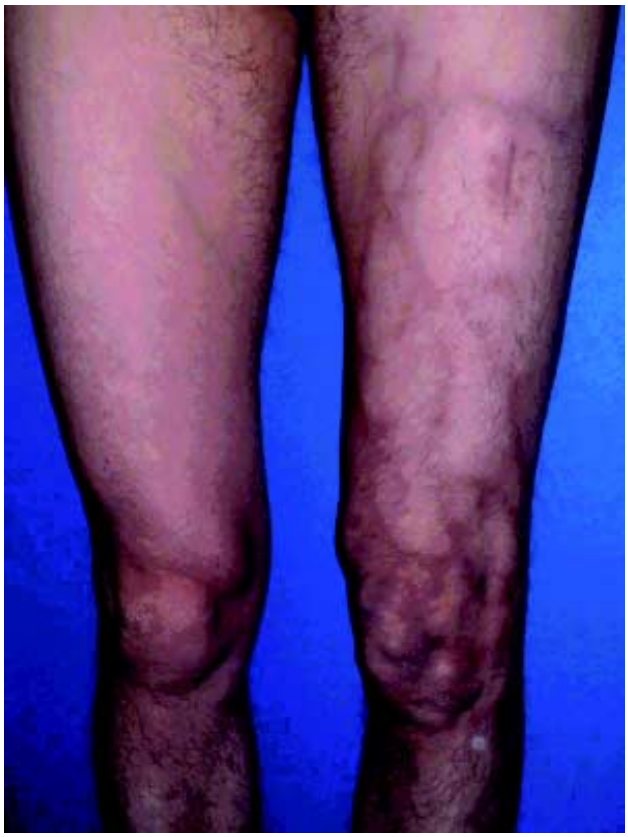

Figure 2. Livedo reticularis and multiple linear post-inflammatory hyperpigmentation over the lower limbs.

medium sized vessel at the dermo-subcutis junction showed marked destruction by polymorphs and multinucleated giant cells with thrombosis. The internal elastic lamina cannot be demonstrated, probably due to marked destruction. The diagnosis of medium sized vasculitis favouring polyarteritis nodosa (PAN) was made.

The patient did not respond to colchicine up to 1.5 mg per day. He was then started on Diclofenac slow-release 100 mg daily and resolution of active lesions was observed. No newly developed lesions were seen on follow-up six weeks later.

Discussion

PAN is a segmental necrotizing, non-granulomatous leukocytoclastic vasculitis that affects small- and medium-sized muscular arteries. It can be divided into systemic and cutaneous form. A comparison of the two forms is tabulated in Table 1.

The cause of CPN is unknown. Various factors have been implicated causing its development which include inflammatory bowel disease,[1,2] tuberculosis,[3] hepatitis B,[4] and streptococcal infections.[5-9]

Typically, CPN presents as painful and tender cutaneous and subcutaneous nodules with livedo reticularis, ulcerations or gangrene. The lower limb is affected in 97.5% of the patients, while the trunk and upper limb are affected in 7.6% and 32.9% respectively. About half of the patients with CPN have skin ulceration, which is associated with severe vascular inflammation and an increased incidence of associated neuropathy.[10] The presence of painful inflamed cutaneous cord-like lesions in our patient was unusual and the clinical differential diagnosis of superficial migratory thrombophlebits has to be considered. The latter however was excluded by histopathology.

Extracutaneously, patients with CPN may have fever, arthralgias, non-destructive arthritis, localised myositis and localised neurological symptoms such as peripheral neuropathy may be present but motor neuropathy is usually not a feature.[10]

The most consistent laboratory abnormalities noted in CPN are elevated ESR (60-94%) and mild anaemia (30%).[11] Immunological tests are not helpful in confirming the diagnosis of CPN but negative results help to exclude systemic vaculitides. Circulating immune complexes and complement activation have not been documented in CPN, except in cases associated with hepatitis B infection. As a result, hepatitis B-associated PAN is generally hypocomplementaemic and appears to be immune complex-mediated.[12] This was illustrated by the association of CPN, hepatitis B infection, cryoglobulinaemia and hypocomplementaemia in the present patient.

Table 1. Comparisons between cutaneous PAN and systemic PAN

	Cutaneous PAN	Systemic PAN
Clinical features	• Painful and tender cutaneous nodules, ulcerations, livedo reticularis or gangrene • Fever, arthralgias, non-destructive arthritis, localised myositis • Localised neurological symptoms • Peripheral neuropathy (50%) • Motor neuropathy usually not a feature	• Cutaneous lesions present in 20% of patients and consist of palpable purpura, nodules, livedo, ulcers. Necrosis and cutaneous gangrene are rare • Hypertension • Visceral involvement • Diffuse neuromuscular involvement
Laboratory investigations	• Elevated ESR (60-94%) • Mild anaemia (30%) • Negative immunological tests help to exclude systemic vaculitides	• Leukocytosis • Eosinophilia • Persistent proteinuria with imparied renal function • Positive immune markers including RF, ANCA, cryoglobulins and decreased complement • Abnormal nerve conduction studies and angiography (renal and mesenteric)
Treatment	• Conservative • Non-steroidal anti-inflammatory drugs • Low or moderate doses of systemic corticosteroids, colchicine, azathioprine, methotrexate, dapsone, hydroxychloroquine	• Aggressive • High dose systemic corticosteroid, cyclophosphamide
Prognosis	• Good prognosis • Relapse and remission course	• Poor prognosis if untreated • Mortality: 85% in 5 years if untreated • 5 years survival: 10% if untreated; 96% if treated

Histologically, there are four stages of development. In the degenerative stage, there are degeneration of the arterial wall with deposition of fibrinoid material and partial or complete destruction of the internal and external elastic laminae. In the acute inflammatory stage, infiltrates mostly composed of neutrophils within the arterial wall are seen. In the granulation tissue stage, infiltrates containing lymphocytes and macrophages with intimal proliferation and thrombosis leading to ulceration can be demonstrated. Finally, fibroblastic proliferation extending to the perivascular area is found in the healed end-stage.[11]

The relationship between systemic polyarteritis nodosa (SPN) and CPN has been proposed by Diaz-Perez et al in 1974 as analogous to discoid lupus erythematosus and systemic lupus erythematosus.[13] The presence of some extracutaneous symptoms such as constitutional upsets, local neurological and musculo-skeletal

manifestations may be associated with CPN without indicating its evolution to SPN. It is suggested by some authors that their relationship is a disease continuum ranging from a skin-limited disease to a life-threatening systemic condition. The progression from CPN to SPN, though rare, may occur and the durations were reported in the literature range from one to twenty years. Hence, systemic involvement needs to be excluded in this patient not only in the first visit but also in subsequent follow-ups.[9]

For CPN, the evaluation of response to treatment is difficult due to the natural fluctuating courses of the disease. Conservative therapeutic plans should be followed. There has been no randomised, double-blinded placebo-controlled trial on the treatment of CPN. And there is no consistent data regarding the steroid – sparing agents of choice. Local measures such as support stockings and local wound care is necessary. Low doses of non-steroidal anti-inflammatory drugs are the first line treatment. Low or moderate doses of systemic corticosteroids may be added in more severe cases. Other drugs reported to be useful include colchicine, azathioprine, methotrexate,[14] dapsone, hydroxychloroquine, pentoxifylline and intravenous immunoglobulin. Prolonged courses of antibiotic therapy may prove helpful in patients with documented streptococcal or other bacterial infections.

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