Case Report

Localized Neurological Necrotizing Vasculitides. Three Cases with Isolated Mononeuritis Multiplex

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ABSTRACT. Localized vasculitic neuropathies are increasingly reported. We describe 3 cases of peripheral neuropathy with necrotizing vasculitis confined to nerves and muscles without systemic involvement. These neuropathies were severe and relapsing, in contrast to a usually benign prognosis. Our cases appear to be isolated vasculitic neuropathies, with vasculitis strictly limited to the peripheral neuromuscular system without nonspecific clinical and/or biological systemic involvement. (J Rheumatol 2001;28:631–3)

Key Indexing Terms:
NECROTIZING VASCULITIS LOCALIZED MONONEURITIS MULTIPLEX

Vasculitis confined to peripheral nerve(s) accounts for up to 30% of all vasculitic neuropathies[1,2]; it usually occurs without fever, weight loss, or serological abnormalities[2,3], and the course of the disease is rather indolent[2].

We describe 3 patients with necrotizing vasculitides limited to small arteries and arterioles of peripheral nerves, and in one case, muscles, but which left the visceral organs intact, without clinical or biological systemic involvement. Our patients suffered relapses or progression despite treatment and one of them died suddenly after one year of impaired deglutition.

CASE REPORTS

Case 1. In December 1995, a 65-year-old woman experienced paresthesia in the fourth and fifth left fingers and weakness of the left hand. Symptoms increased progressively until May 1997, when she complained of paresthesia in both hands and across the sole of the left foot. Neurological examination showed motor impairment in the ulnar and median regions, sensory loss in the sural region of the left foot, and attenuated ankle jerks.

Standard blood tests and serological tests for hepatitis C virus (HCV) and Lyme disease were negative. Hepatitis B surface antigen (HBsAg) was absent, but antibodies to hepatitis B core antigen and HBsAg were detected. Cerebrospinal fluid (CSF) examination was normal. Electromyography (EMG) detected bilateral, asymmetric, distal, sensorimotor, axonal polyneuropathy, normal sensory and motor conduction velocities, and abnormal sensory and motor nerve action potentials in clinically involved regions and in the right median and ulnar regions. A right peroneal neuromuscular biopsy revealed chronic and recent denervation processes in the muscle and axonal degeneration, demyelinization, and fibrinoid necrosis of 2 medium size epineurial arteries associated with transmural infiltration with lymphocytes and mononuclear cells, and partial occlusion of the lumen.

Treatment with prednisone (1 mg/kg/day) was started in November 1997. One year later, she was taking 5 mg/day of prednisone and still complaining of tremors and ataxia in her hands, without attenuation of the clinical symptoms.

Case 2. In 1988, a 51-year-old man progressively developed sensory impairment of the right ulnar and radial nerves, then the left femoral nerve. In 1990, he was still complaining of paresthesia of the ulnar border of the palm and the fifth finger of the right hand, and presented with impaired sensation in the left sural region, complete paralysis in the right radial region, palsy in the right ulnar region, left peroneal muscle involvement, and no left knee or ankle jerks.

The standard blood tests were normal, and autoantibodies, cryoglobulin, and serological tests for hepatitis B virus (HBV), HCV, human immunodeficiency virus (HIV), and Lyme disease were negative. CSF protein level was elevated at 0.50 g/l, with normal electrophoresis and no cells. EMG showed bilateral asymmetric sensorimotor axonal polyneuropathy with abnormal sensory and motor nerve action potentials in clinically involved regions and in the left median, right tibial, and sural regions. A left peroneal neuromuscular biopsy revealed atrophy and perivascular hemosiderin deposits, myelinated fiber loss, and healing of necrotizing vasculitis. Several epi- and endoneurial small vessels showed fibrotic thickening of vessel walls, sometimes leading to partial or complete occlusion of their lumens. One medium size epineurial artery had focal necrosis with eosinophilic deposits in the wall. No inflammatory infiltrates were observed in nerve or muscle.

Despite 2 months of treatment with oral prednisone (1 mg/kg/day) neurological status was unchanged, and oral cyclophosphamide (100 mg/day) was prescribed for one year. When therapy was stopped, deficits remained unchanged.

In December 1995, he developed hypoesthesia in the region supplied by

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the mandibular branch of the left trigeminal nerve, left peroneal weakness, and loss of all tendon reflexes except the triceps. All blood tests were negative. He refused treatment with plasma exchanges and was lost to followup in 1997.

Case 3. Since 1992, a then 60-year-old man complained of pain on the left side of his face and the right hip and a gait disturbance. In 1994, he described sensations of walking on straw across the sole of his left foot, reported girdle sensations of the legs, painful paresthesias of the left leg and the left half of his face, and urinary incontinence. Neurological examination detected hyperesthesia over the left half of his body, and impaired vibratory sense in his left leg and posture sense in his left toes. Standard blood tests were normal. CSF examination showed proteins at 0.53 g/l with normal electrophoresis and no cells. Cerebral and lumbar magnetic resonance images were normal. In January 1997, sensory impairment had progressed to both legs and his left forearm and hand. Creatine phosphokinase (CPK) was 510 IU (N < 170). Serological tests for HCV, HBV, HIV-1 and -2, TPHA-VDRL, and antineutrophil cytoplasmic antibodies were negative. EMG showed proximal and distal, bilateral, diffuse, predominantly motor, symmetric axonal polyneuropathy with denervation. A left peroneal neuromuscular biopsy revealed marked atrophy, infiltration with mononuclear cells and lymphocytes, and fibrinoid necrosis of medium size arteries (Figure 1). In the nerve, axonal loss with acute wallerian degeneration, epineural perivascular inflammatory infiltrates, and endoneural infiltration with polymorphonuclear cells were observed.

Prednisone (1 mg/kg/day) was started. One month later, neurological symptoms worsened. He received intravenous (IV) cyclophosphamide (1 g/mo) for 4 months, together with plasma exchanges (3/week) for 4 weeks followed by intravenous immunoglobulins (IVIG) (2 g/kg once a month). In August 1997, he was taking prednisone (20 mg/day); IV cyclophosphamide and IVIG were stopped and oral cyclophosphamide (150 mg/day) was initiated. In November, pain, hypoesthesia, and distal weakness increased and he could walk only with the aid of crutches. Deglutition impairment increased. Cyclophosphamide was stopped; prednisone (20 mg/day) was continued in combination with cyclosporine (3 mg/kg/day). He died in March 1998.

DISCUSSION

Our 3 patients had histologically proven necrotizing angiitis. Although the absence of antineutrophil cytoplasmic antibodies was suggestive of polyarteritis nodosa, histological findings were nonconfirmatory.

Clinical presentation, EMG, and histological features of our cases of nonsystemic vasculitic neuropathy were consistent with those described[2,4], i.e., multifocal neuropathy of sudden onset[5,6], or distal asymmetric and/or symmetric polyneuropathy of gradual evolution[2,4-9]. The dominant finding seen in nerve biopsies from patients with vasculitic neuropathy is axonal degeneration, with low amplitude sensory and compound muscle action potentials with minimal reduction of conduction velocities[6,8,10].

Under treatment, neurological deficit usually regresses slowly, sometimes with marked sequelae[7]. In most series, the prognosis of isolated nerve vasculitis in terms of survival and functional recovery was reportedly better than for the more generalized vasculitides[2,7,9,11]. Our patients, however, did not improve under therapy: all suffered relapses or progression, and one died. Thus, necrotizing vasculitis localized to nerves and/or muscles with few histologically confirmed inflammatory changes may have a poorer prognosis than reported. These cases are probably more resistant to steroids and cytotoxic therapy owing to the milder inflammatory involvement and absence of general systemic inflammatory signs.

We agree with others[4,12] that most cases of isolated vasculitic neuropathies are vasculitic processes localized to the peripheral nervous and/or muscle system. Some authors consider that localized vasculitis is not an organ-specific vasculitis like cutaneous vasculitis, but rather a mild form of vasculitis; moreover, systemic necrotizing vasculitis is thought to possibly develop later[1,4]. We agree[2] that isolated

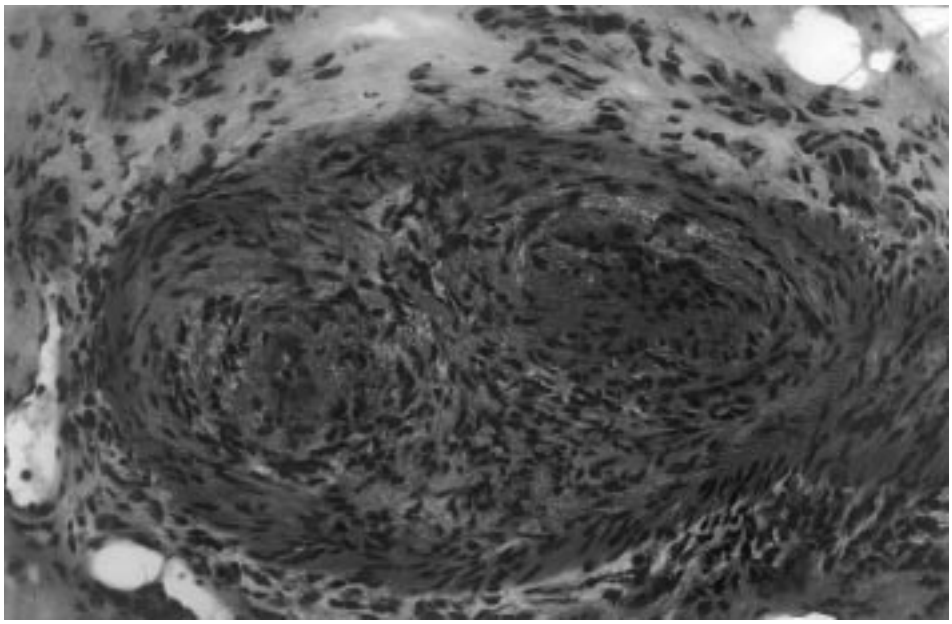

Figure 1. Muscle biopsy of Patient 3. Necrotizing arteritis affecting a medium size artery at the level of a bifurcation. (hematoxylin and eosin; original magnification ×360).

vasculitic neuropathy is a tissue-specific vasculitic disorder affecting nerve and/or muscles since, despite longterm followup in many studies[7,12], no patients developed additional systemic vasculitic symptoms.

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