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INCLUSION BODY MYOSITIS AND HIV INFECTION

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Neurological disorders are frequent complications of human immunodeficiency virus (HIV) type 1 infection, and include central nervous system (CNS) infections, neoplasm, vascular complications, peripheral neuropathies, and myopathies[1]. Early series emphasized CNS diseases, with relative few reports of primary disorders of peripheral nerve and muscle[2]. Myopathy may occur at any time during the course of HIV infection and is not associated with any particular stage of immunosuppression[3]. Before the introduction of zidovudine (azidothymidine, AZT) for the treatment of AIDS, muscle disease was considered a rare complication of HIV, found in less than 1% of cases of AIDS[2]. A variety of muscular disorders has been described in HIV infected patients[3]: polymyositis, myopathy induced by nucleoside reverse transcriptase inhibitors (NRTI), such as zidovudine, opportunistic infections including toxoplasmosis, infiltration by tumour, HIV associated vasculitis, and rhabdomyolysis caused by HIV itself or by drugs including didanosine[5]. A myopathy in every respect similar to inclusion body myositis (IBM) is observed in rare patients infected by HIV-1 or human T-cell leukaemia virus type 1(HTLV-1)[6,7]. IBM is a chronic inflammatory muscle disease, and the typical clinical findings are muscle weakness and atrophy, most prominent in the quadriceps muscles and the wrist and finger flexors[8].

We report a case of a male patient, who presented with signs and symptoms of IBM in association with HIV infection.

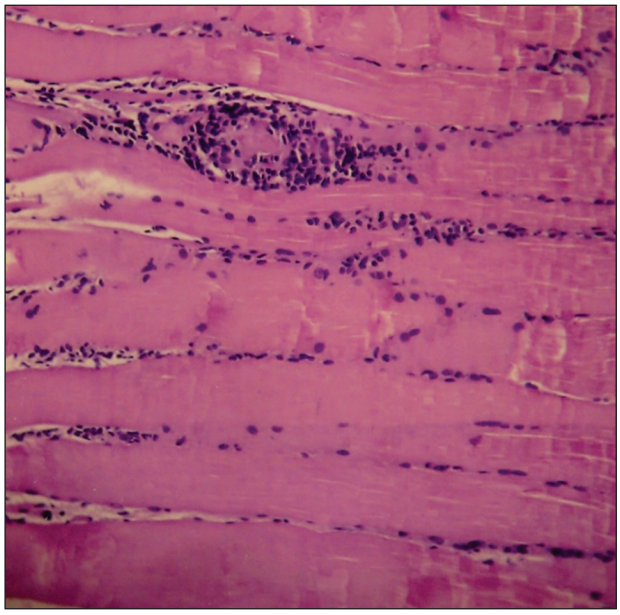

Fig 1. Paraffin section stained with H&E showing endomysial lymphocytic foci (x100).

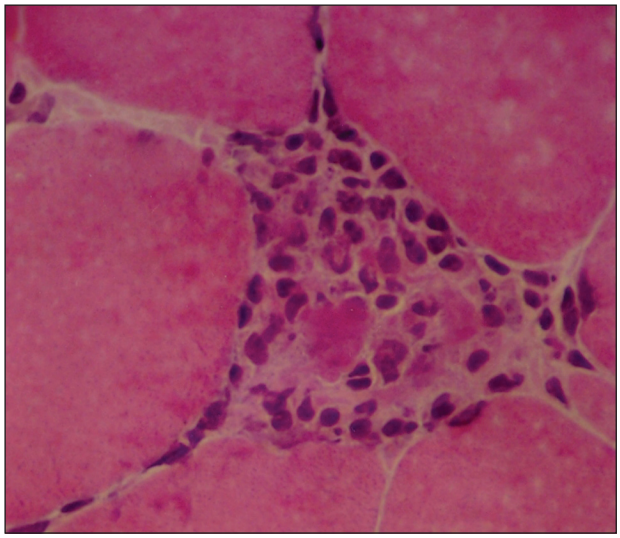

Fig 2. Frozen section stained with H&E showing a necrotic fibre infiltrated by macrophages and lymphocytes (x400).

CASE

A 56 year-old French man was diagnosed as having HIV infection in 2000. Initially the CD4 cell counts were 314 and the viral load was 626 copies. A treatment with HAART was started. Two months later the CD4 was normal and the viral load fell to 0. One year later he noticed difficulty in climbing stairs with slowly progression and in seven months he could walk only with aids of canes. He also noticed some difficulties with movements of the hands. A diagnostic of a muscle disease due to zidovudine was done and HAART was stopped. As there was no improvement in

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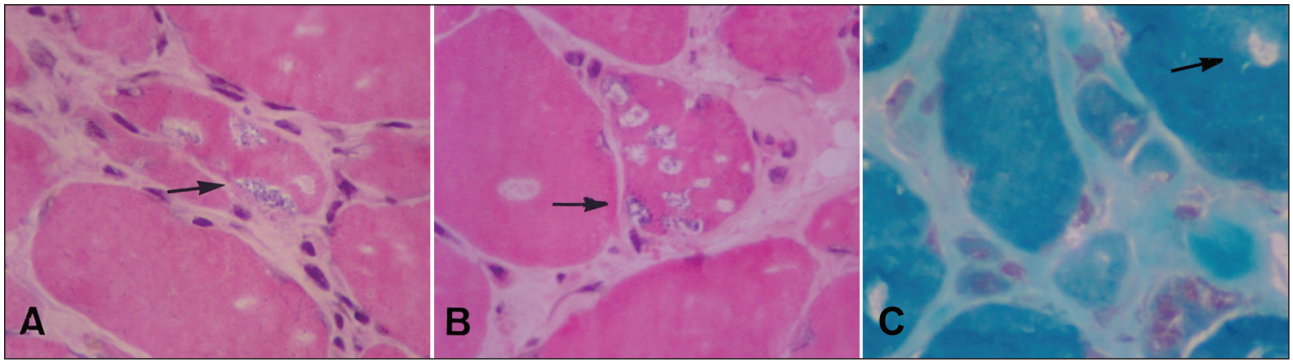

Fig 3. Sections stained with H&E (A, B) and Gomori's trichrome (C) showing fibres with rimmed vacuoles (x400) (arrow).

eight months the patient was referred to our service. The physical examination was normal. There was proximal muscle atrophy in lower limbs mainly in the quadriceps. The strength was diminished in proximal and distal muscles in lower limbs. In the upper limbs the weakness was localized in the hands, mainly in wrist and fingers flexor muscles (Table 1). The patellar reflexes were abolished and the ankle reflexes were diminished. In the upper limbs the tendon reflexes were normal. The sensory and the cranial nerves examination were normal. The blood biochemical examination was normal except for a CK of 2600 U. The EMG examination revealed increased spontaneous activity, with fibrillations, complex repetitive discharges and positive sharp waves. The motor units had low-amplitude polyphasic units, usually of short duration. A muscle biopsy was performed. Histochemical stains were done. Muscle fibres were irregular in size and shape; there were many atrophic fibres, some of them angulated, and mild increase in endomysial collagen. Endomysial lymphocytic foci (Fig 1) and necrotic fibres infiltrated by macrophages (Fig 2) were present, as well as some fibres containing rimmed vacuoles (Fig 3A,B), also shown with the Gomori's trichrome (Fig 3C). The treatment consists of Immunoglobulin IV (IVIg) 400 mg/kg/day for five days. The muscles weakness improved slowly and the CK decreased to 367 U (Table). The IVIg infusion was done once a month. After five months of IVIG, the muscle weakness became stable till the last examination in 2007, August.

Table. Strength examination (MRC) and CK.

Muscle	First day of admission		Five months after IVIg	
Abductors of the shoulder	R 5	L5	R 5	L5
Extensors of the forearm	R 5	L5	R 5	L5
Flexors of the arms	R 5	L5	R 5	L5
Flexors of the fingers	R 3	L 3	R 4	L4
Abductors of the fingers	R 5	L5	R 5	L5
Extensors of the thigh	R 3	L3	R 4	L4
Flexors of the thigh	R 3	L3	R 4	L4
Extensors of the legs	R 4	L4	R 5	L4
Adductors of the thigh	R 5	L5	R 5	L5
Extensors of the foot	R 0	L0	R 1	L1
Flexors of the foot	R 2	L2	R 4	L4
Extensors of the toes	R 0	L0	R 1	L1
CK (U)	2600		367	

R, right; L, left.

DISCUSSION

IBM is one of the three main subsets of inflammatory myopathies, the other two being polymyositis and dermatomyositis[8], and it's considered the most common acquired, progressive and disabling myopathy in patients above the age of 50 years, and has a male predominance[8].

IBM has a slow progression, affects both the proximal and the distal muscles. The amyotrophy can be asymmetric, and in typical cases muscle weakness and wasting are most profound in knee extensors, hip flexors and long finger flexors[8]. Most patients require an assistive device within several years of onset[9]. Neck flexors and extensors and facial muscle are frequently affected[8]. The muscles of swallowing are affected in about 50% of the patients[8]. The tendon reflexes can diminish in later stages when the atrophy of major muscle groups becomes evident[8]. Our case had the typical clinical findings of IBM.

Creatine kinase (CK) levels can initially be elevated up to 10-fold and remain slightly elevated as the disease progresses. In our case the CK was very high what is described in IMB associated with retrovirus[6]. The EMG of our patient is typical of muscle affection.

The main histological features are red-rimmed vacuoles, endomysial T cell infiltrates, cytoplasm inclusions, atrophic fibres and amyloid deposits[6]. The inflammatory infiltrates consist of CD8+ T cells and macrophages, suggesting involvement of a T cell mediated cytotoxic mechanism against muscle fibres[10]. Although we could not perform techniques for amyloid, as specific antibodies against beta amyloid or immunocytochemical analysis

and ultrastructure techniques, the morphological changes seen in our case, particularly the lymphocytic infiltration and the rimmed vacuoles, although non-specific, are highly suggestive of IBM.

The aetiology of IBM is unclear. The immunopathological findings suggest an immune-mediated process but the lack of response to immunotherapy and the amyloid deposits have raised the possibility of a degenerative disorder. Viral aetiologies have been suggested[11]. A few reports of HIV or HTLV-1 positive patients with IBM indicates that the disease is more common in patients who live longer and harbour this virus for several years[6,12]. The IBM in HIV infected patients is like to the sporadic IBM, except for the earlier age of onset and the higher elevation of muscle enzymes[6].

The mechanism by which the retrovirus triggers the disease is unclear. Retroviral antigens have been detected in endomysial macrophages but not within the muscle fibers[6,7]. The activated CD8+ cells invade muscle fibres expressing MHC class I, as seen in retrovirus-negative polymyositis and IBM[6,11]. These cells are retrovirus-specific, because their CDR3 region contains amino acid residues that are specific for viral peptide bound to HLA molecules[12].

The myopathy due to AZT is different from IBM. It's presumably due to an interference with mitochondrial function[4]. Typical features of this myopathy are ragged red fibres and paracrystalline inclusions in mitochondria that have been attributed to its DNA (mtDNA) depletion[13]. Ragged red fibres may be seen in rare cases of IBM suggesting that mitochondrial function is impaired in this disease[10].

A direct link between NRTI, mitochondrial dysfunction, and IBM is strongly suggested in a case of IBM in HIV infection[7] NRTI prolonged use may contribute to the development of IBM in this type of patients. In these cases the discontinuation of NRTI may be a strategy for management, although whether the condition is reversible remain unknown[7].

Because there is no effective medical treatment in IBM (steroid and other immunosuppressive treatments have disappointing results), all other measures that could possibly be of benefit to patients should be considered[8]. Some authors think that IVIg may be useful for treatment of IBM[14]. Our patient showed a modest but permanent improvement with IVIg 400 mg/day for five days and one month infusion for one day. Mild to moderate muscle training or aerobic endurance training, can be performed without adverse effects[15].

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