Rare disease

Brachial amyotrophic diplegia in the setting of complete HIV viral load suppression

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Summary

Brachial amyotrophic diplegia (BAD) is a rare segmental form of motor neuron disease which presents with asymmetric lower motor neuron weakness largely confined to the upper extremities (UE). In the case being reported, a 62-year-old gentleman on antiretroviral treatment since 1993, presented with left-arm weakness in 2007 that quickly progressed to involve the right arm. Complete HIV-viral load suppression had been achieved since 2003. Examination revealed lower motor neuron weakness in both UEs, worse proximally than distally and normal strength in the lower extremities (LEs). Nerve conduction studies showed reduced amplitudes of bilateral median and ulnar nerves' motor responses. Needle electromyography of bilateral UE showed active and chronic denervation/reinnervation changes with normal findings in both LEs. MRI of the cervical spine showed cord atrophy. This is the first case report describing a patient who presented with BAD in the setting of complete HIV-viral load suppression for many years.

BACKGROUND

Motor neuron disease is a heterogeneous group of disorders, the most common form being amyotrophic lateral sclerosis (ALS). In ALS, both upper and lower motor neurons are involved in the same patient. However, other phenotypes of motor neuron disease involve either only the upper motor neurons (eg, primary lateral sclerosis) or only the lower motor neurons (eg, progressive spinal muscular atrophy). In the latter category of disorders, a rare segmental variant that is called brachial amyotrophic diplegia (BAD) has been described. Initially called flail arm syndrome, this condition is also known by a number of other names including Vulpian-Bernhardt syndrome, hanging-arm syndrome, neurogenic man-in-a barrel syndrome and segmental proximal spinal muscular atrophy. Since 1985, about 23 cases of motor neuron disease associated with HIV have been documented in the literature. Only two of these cases had the BAD phenotype with both patients described being newly diagnosed HIV patients.^{1 2} We here describe a case of a patient with HIV viral load suppression for years, who presented with BAD.

CASE PRESENTATION

A 62-year-old gentleman diagnosed with HIV 20 years ago, achieving complete viral load suppression 11 years later on HAART, first complained of left arm weakness in 2007. He initially reported difficulty lifting his left arm with similar symptoms soon also affecting his right arm. Over the following years, his weakness slowly progressed with significant weakness in the upper extremities. He also noticed diffuse twitching in both his arms. Minimal proximal involvement of the lower extremities occurred clinically 3 years after the onset of symptoms.

His general physical exam was unremarkable. Cranial nerve examination was normal, with no tongue atrophy or fasciculations noted. Motor exam showed severe atrophy in

the periscapular area bilaterally, moderate to severe atrophy in the forearm and intrinsic hand muscles bilaterally. Muscle tone was mildly reduced in both upper extremities and normal in the lower extremities. There was no percussion, action myotonia or paramyotonia. Manual muscle testing revealed medical research council grade: shoulder flexion and extension 1/5 bilaterally, elbow flexion and extension 3/5 bilaterally, abductor pollicis brevis, adductor digiti minimi and first dorsal interosseous were all 3/5 bilaterally. Occasional fasciculations were noted in both upper extremities. In the lower extremity, strength was initially normal. Deep tendon reflexes were absent at the biceps, triceps and brachioradialis bilaterally, 2+ at the knee joint bilaterally and trace at the ankles bilaterally. Three years later, the patient developed mild weakness of neck extension (4/5), as well as hip flexion and extension (4/5).

INVESTIGATIONS

Nerve conduction studies and needle electromyography (EMG) carried out 6 months after the onset of his symptoms showed normal sensory studies. Motor studies of bilateral median nerves showed mildly reduced distal amplitudes with borderline-prolonged distal motor latencies (DML) but normal forearm conduction velocities. The left ulnar motor response showed mildly reduced distal amplitude with normal DML and normal conduction velocities. The right ulnar and right peroneal motor conduction studies were normal. Needle EMG of bilateral upper extremities showed active denervation with fibrillation potentials (FPs) and positive sharp waves (PSWs) as well as chronic neurogenic changes (high-amplitude, long-duration rapidly firing polyphasic units) of C5 through T1 myotomes bilaterally though the left side was worse than the right. FPs and PSWs were also seen in the cervical paraspinal muscles. Needle EMG of the lower extremities was essentially normal.

Figure 1 Sagittal T2-weighted image showing cervical cord atrophy.

His blood workup included screening for antinuclear antibodies, antinuclear cytoplasmic antibodies, rheumatoid factor, antiganglioside antibodies, anti-GQ1b and anti-GD1a antibodies, cryoglobulins, heavy metals, hexosaminidase A, porphyria and acid maltase levels (Pompe disease). These were all negative. A complete blood count, thyroid stimulating hormone, serum protein electrophoresis with immunofixation and vitamin B12 levels were also normal. Creatine kinase had been elevated for many years up to 1932U/l. Inflammatory markers had been repeatedly normal. Syphilis and lyme titres were also negative. CD4 count ranged between 450 and 568 cells/ μ l (normal value: 370–1540 cells/ μ l) over a 3-year period. A lumbar puncture was performed showing normal protein of 27 mg/dl and glucose of 62 mg/dl. There were no white cells in the cerebrospinal fluid with only three red blood cells seen. Oligoclonal bands and John Cunningham (JC) virus were not detected, lyme and syphilis were both negative. An MRI of the cervical spine with and without gadolinium

showed mild atrophy of the cervical cord throughout its course with moderate-to-severe bilateral foraminal narrowing but no cord signal abnormality (figures 1 and 2). No abnormal enhancement was noted.

DIFFERENTIAL DIAGNOSIS

Since bilateral arm weakness can be the presenting feature of ALS early on, it may be difficult to distinguish between the two. What may help distinguish the two phenotypes is the fact that distal weakness and pyramidal tract involvement are more typical of ALS.³ In contrast, the lack of bulbar signs with sparing of lower extremity muscles and initial EMG findings limited to cervical myotomes is more typical of BAD. Katz *et al*⁴ in their series of patients with BAD set the inclusion criteria to make a diagnosis of BAD at 18 months during which weakness was restricted to the upper extremities. It is important to distinguish between the two disorders since patients with BAD have a median survival of 58 months which represents a longer survival trend than ALS.

TREATMENT

The patient was started on riluzole twice a day, was being followed by the pulmonary lab watching his respiratory status and having regular sessions of physical and occupational therapy.

OUTCOME AND FOLLOW-UP

Unfortunately, the patient also had multiple medical comorbidities and he passed away 5 years after the onset of symptoms after being diagnosed with oesophageal cancer.

DISCUSSION

BAD is classified as a segmental lower motor neuron disease characterised by severe bilateral upper extremity weakness unaccompanied by pyramidal, bulbar or lower extremity abnormalities for at least 18 months from the onset of symptoms.⁴ Progression to other regions clinically or electrodiagnostically beyond this time frame, as occurred in our patient, has been described, pointing to a slowly progressive motor neuron disorder. However, if upper motor neuron signs develop, this would then fall under the ALS spectrum.

Figure 2 Axial T2-weighted sequence at the level of C6. On the left is a sequence from our patient showing cord atrophy. On the right is a normal cervical spine MRI through the same level for comparison.

This is the first case report of a patient with BAD who had an HIV viral load that had been controlled for many years. The association of HIV and ALS has been well described in the literature.⁵ ALS associated with HIV differs from sporadic ALS in earlier age of onset, more rapid progression and some improvement with antiretroviral therapy.⁶ Whether HIV has a direct causative effect in the development of motor neuron disease or this is just coincidental is not clear. HIV is not neuronotropic though it infects glial cells.⁷ How this could be pathogenic to the anterior horn cells is unknown. Different pathogenic mechanisms have been described that could lead the HIV to cause anterior horn cell damage. These include direct damage caused by the HIV itself, the result of cytokines and chemokines released secondary to HIV infection, the release of neurotoxic HIV proteins (such as gp120, gp41, tat) or damage resulting from opportunistic infections.^{7,8} The literature on HIV associated with BAD is very limited since only two cases have been described. The fact that, in our patient, the HIV viral load had been undetectable for many years prior to the onset of his symptoms points to more of a coincidental rather than causative role. This is reinforced by the fact that in HIV-associated ALS the prevalence of ALS does not seem to exceed what would be observed by chance alone. However, more studies are needed to determine whether HIV plays a role in the development of BAD.

Learning points

- ▶ Brachial amyotrophic diplegia (BAD) is a rare segmental form of motor neuron disease which presents with asymmetric lower motor neuron weakness of the upper extremities without upper motor neuron signs, bulbar or lower extremity involvement.
- ▶ Distinguishing features favouring BAD over amyotrophic lateral sclerosis (ALS):
 - Lack of bulbar signs;
 - Lack of involvement of the lower extremity for at least 18 months from the onset of symptoms;
 - No upper motor neuron signs.
- ▶ BAD has a better prognosis than ALS.
- ▶ Electromyography (EMG) is helpful in characterising the distribution of the disorder and following up the progression of the disease.
- ▶ The role of HIV in the pathogenesis of motor neuron disease is unclear and further studies are required to clarify this.

Competing interests None.

Patient consent Obtained.

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Cachia D, Izzy S, Ionete C, Salameh J. Brachial amyotrophic diplegia in the setting of complete HIV viral load suppression. *BMJ Case Reports* 2012;10.1136/bcr-2012-007632, Published XXX

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