Patient 3 in our study had a sudden onset of irregular fluctuating tremor suggestive of functional origin. It was supported by distractibility and complete amelioration of tremor by a placebo injection. Although functional tremors usually affect the limbs, in some patients, shaking of the head and face may occur.[12] However, to the best of our knowledge, no patient has been reported with functional tremor involving the suprahyoid region of the neck.

We described three patients presenting with tremors involving the suprahyoid region of the neck. In such patients, it is necessary to investigate their medication history and to search for clinical features suggestive of psychogenic origin.

LEGENDS TO THE VIDEO

Segment 1. (Case 1) An 82-year-old man shows anterior upper neck muscles tremor at rest. There is no tremor of the tongue when he speaks or opens his mouth, but videofluroscopy studies show the posterior tongue tremor.

Segment 2. (Case 2) An 85-year-old man shows anterior upper neck muscle tremor. This tremor was observed only at rest. Two weeks after the discontinuation of levosulpiride treatment, the tremor disappears completely.

Segment 3. (Case 3) A 56-year-man shows irregular anterior upper neck tremor at rest. The tremor disappears completely after a placebo injection.

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Genetically Confirmed Huntington's Disease Masquerading as Motor Neuron Disease

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Video 

Abstract: **We describe a patient with Huntington's disease (HD) who showed asymmetrical upper limb amyotrophy as a main manifestation. Chorea and psychiatric symptoms were not prominent. Electromyography revealed generalized active and chronic denervation and fasciculations. A genetic test showed 46 CAG repeats in the *huntingtin* gene. Asymmetrical amyotrophy restricted to the upper limb has been reported in some patients with progressive chorea and amyotrophy without acanthocytosis, but genetically proven cases of HD have rarely been reported. It is not known why only a few HD patients show the motor neuronal loss; however, certain as-yet-unidentified genetic factors combined with some environment factors and the underlying cellular dysfunctions by polyglutamine aggregation could be responsible for the motor neuronal loss similar to that in amyotrophic lateral sclerosis.**

Key words: Huntington's disease; amyotrophic lateral sclerosis; polyglutamine disease; motor neuron disease; asymmetric atrophy.

Huntington's disease (HD) is an autosomal-dominant neurodegenerative disorder that is associated with the

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expansion of a trinucleotide repeat in the *huntingtin* gene.[1] HD is characterized by progressive chorea, rigidity, and dementia; however, involvement of the motor neurons in genetically proven cases is uncommon. We herein describe an HD patient who showed muscular atrophy in the upper extremities as an initial and main manifestation. Electrodiagnostic studies provided evidence of generalized active and chronic denervation with fasciculation potentials, indistinguishable from those in patients with amyotrophic lateral sclerosis (ALS).

CASE REPORT

A 41-year-old man experienced muscle weakness and atrophy in the left arm and hand. One year later, he noticed slight involuntary movements in the upper extremities and trunk. The weakness and muscular atrophy were progressive and spread to the left proximal arm muscles. At the age of 47, he had marked muscular weakness and atrophy in the left distal upper limb with mild choreic movement in his face, upper extremities, and trunk. He was referred to our hospital at the age of 48. A detailed history showed that his father and siblings had what appear to be involuntary movements in the limbs in their 60s, but they did not have dementia or psychotic symptoms. On examination, the man was alert and cooperative with slightly decreased mental function (MMSE 29/30). He showed very mild chorea mainly in the distal upper limbs (Supplementary-Video), which was exacerbated by mental load such as counting. He also showed slight dysarthria with equivocal tongue atrophy. Severe amyotrophy was noted in the dorsal interosseous and thenar muscles, and moderate atrophy in the arm and shoulder girdle muscles on the left (see Fig. 1). In addition, mild atrophy was seen in the right intrinsic hand muscles. On the Medical Research Council scale, his muscle strength in the left upper limb was graded as 3/5 for the biceps brachii, triceps, and wrist extensor and flexor muscles, 2/5 for the deltoid and finger extensor muscles, and 1/5 for the abductor pollicis brevis and dorsal interosseous muscles. Muscle strength in the right upper limb was graded 4+/5 except in the intrinsic hand muscles (graded as 4/5). Fasciculations were present in the shoulder and arm muscles, bilaterally. Hyperreflexia was noted in all the four limbs, and plantar responses were flexor. His sensory examination was normal.

The Japanese version of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) revealed that he had mild cognitive disturbance (FIQ = 78).

Brain magnetic resonance imaging (MRI) revealed mild diffuse cortical atrophy, but no obvious atrophy of the caudate nuclei. Cervical MRI showed only slight spondylotic change in cervical spine. Single-photon emission computed tomography showed mildly decreased blood flow in the frontal cortex.

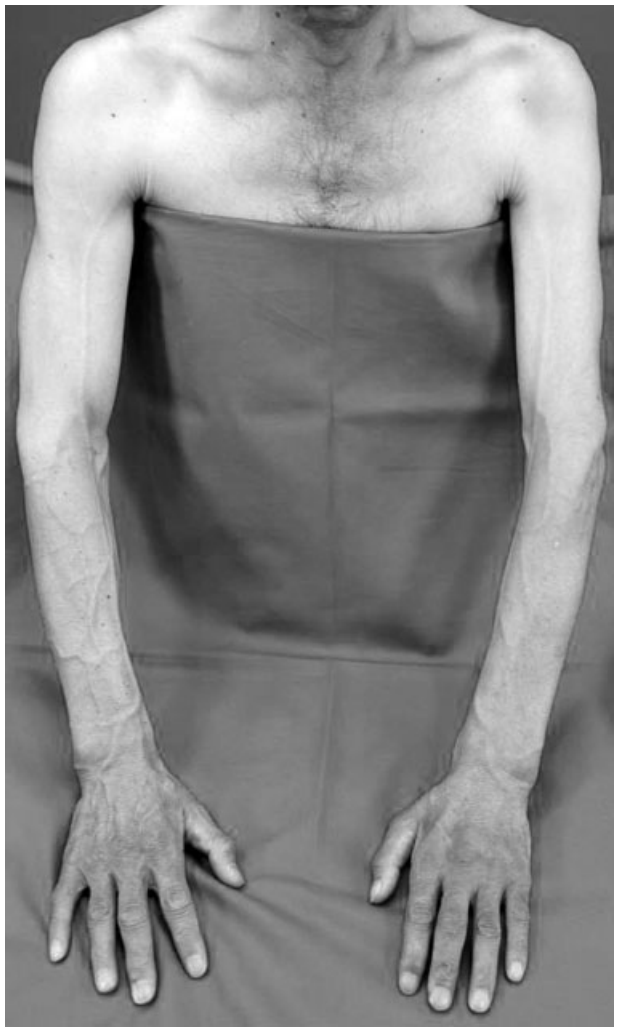

FIG. 1. Muscle atrophy in the upper extremities. On the left, diffuse amyotrophy from the shoulder girdle to the hand can be seen. On the right, amyotrophy was predominant in the small hand muscles.

His clinical and electrodiagnostic features (see later) fulfilled the diagnostic criteria for probable ALS. Gene tests, however, revealed abnormal CAG expansion with 46 CAG repeats in the *huntingtin* gene.

ELECTROPHYSIOLOGY

Nerve conduction studies showed a severe decrease in amplitudes of compound muscle action potentials (CMAPs) in the left median (1.3 mV; normal $>$ 5 mV) and ulnar (1.3 mV; normal $>$ 4.5 mV) nerves and in the right median nerves (1.6 mV). CMAP amplitudes in tibial and peroneal nerve studies were normal on both

sides. Amplitudes of sensory nerve action potentials and sensory nerve conduction velocities were entirely normal in the bilateral median, ulnar, and sural nerves. Electromyography was systematically performed in the tongue and left deltoid, flexor carpi radialis, first doral interosseous (FDI), T10-paraspinalis, and vastus lateralis muscles. It showed evidence of diffuse active and chronic denervations. Fibrillation potentials were present in the deltoid, FDI, and T10-paraspinalis, whereas fasciculation potentials were found for all the muscles tested. Changes in motor unit potentials including polyphasia and long-duration were observed in all the muscles examined. Findings suggesting unstable neuromuscular transmission (jitter/blocking of polyphasic spikes) were seen in the tongue, deltoid, FDI, and T10-paraspinalis. Therefore active or chronic denervation was found for the cranial, cervical, thoracic, and lumbar segments.

DISCUSSION

Our patient's case was characterized by prominent upper limb amyotrophy and generalized hyperreflexia with electrophysiological evidence of widespread denervation and fasciculations. The patient's condition fulfilled the El Escorial ALS criteria.[2] Gene tests, however, revealed abnormal CAG expansion in the *huntingtin* gene, leading to the diagnosis of HD, while the phenotype appeared to be that of motor neuron disease. If family history of chronic choreic syndrome had not been disclosed, the diagnosis of HD could have been missed.

HD and ALS are both relatively rare neurodegenerative disorders. Nevertheless, previous reports have shown several patients with coexistence of HD and motor neuron syndrome,[3] initially described by Fotopulos.[4] Molecular diagnosis for HD became available only after 1993; since then several patients showing chorea and amyotrophy with no acantocythosis and no expanded CAG repeats in *IT15* gene have been reported,[5,6] but only a few patients with genetically confirmed HD along with ALS-like features have been reported.[3,7] Hence the association between HD and amyotrophy in the reports before 1993 seems to be uncertain.

Some symptoms in this case were similar to those of the previously reported cases showing progressive chorea and amyotrophy. Shoulder girdle atrophy, which was observed in this case, was often seen in patients with progressive chorea and amyotrophy without acanthocytosis. Furthermore, prominent amyotrophy in this case was restricted to the upper limbs asymmetrically; this was also seen in some similar patients in previous reports. In familial ALS with *SOD1* mutations, an initial manifestation is often focal and asymmetric amyotrophy of the unilateral hand, with spread in a contiguous manner[8]; this asymmetric amyotrophy is also seen in this case and previously reported cases of possible Huntington disease with amyotrophy. The precise reason for the similarity is still unclear; however, similar molecular mechanisms could be responsible for similarity in the symptoms.

There are several possible mechanisms of motor neuronal loss in HD. It is generally thought that the cytotoxicity of abnormally prolonged CAG repeats in the *IT15* gene is brought about by the aggregation of prolonged polyglutamine (polyQ) peptides in neurons.[1] It is also supposed that such polyQ aggregation eventually leads to various cellular dysfunctions (transcriptional dysregulation, proteasome impairment, and mitochondrial dysfunction).[9] Because Bunina bodies have occasionally been observed in the anterior horn cells of HD patients,[3] the aggregation of prolonged polyQ in the motor neurons would trigger neuronal dysfunction and death as seen in ALS.

This case demonstrates that clinical and electrodiagnostic features mimicking ALS could be the main manifestation of patients with HD, even if the typical clinical features of HD, such as chorea, personality changes, dementia, and extrapyramidal symptoms, are less prominent. It is not known why only a few HD patients show the motor neuronal loss. The association may be coincidental; however, certain as-yet-unidentified genetic factors combined with the underlying cellular dysfunctions caused by polyQ aggregation could be responsible for the motor neuronal loss similar to that seen in ALS. Recently, studies on monozygotic twins who share the same CAG expansion in *IT15* revealed the importance of environmental factors for phenotype expression of HD.[10] Such environmental factors would also contribute to a rarely observed motor neuronal loss and a phenotypical heterogeneity in HD.

LEGENDS TO THE VIDEO

Segment 1. Very mild chorea in the distal upper limbs.

Segment 2. Chorea exacerbated by mental load.

Segment 3. Amyotrophy and weakness in the upper limbs.

Segment 4. Slight dysarthria.

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Aceruloplasminemia: A Novel Mutation in a Family with Marked Phenotypic Variability

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Video 

Abstract: **Hereditary aceruloplasminemia (HA) is a rare inherited disease characterized by anemia, iron overload, diabetes, and neurodegeneration. HA is caused by the homozygous mutation of the ceruloplasmin (CP) gene. We report two siblings with markedly different phenotypes carrying a novel mutation: a homozygous deletion of two nucleotides (1257–1258 TT del) causing the premature stop of the Cp protein translation (Y401X). An early diagnosis of iron overload was made in the female sibling who was subsequently treated with deferoxamine. At the age of 54, her neurologic symptoms were limited to mild akinetic signs and a history of seizures; moreover, her fasting blood glucose level never exceeded 120 mg/dL. The male sibling, who had not received any specific treatment for HA, developed severe diabetes at the age of 32 and at 48 manifested a progressively disabling neurologic disease. Possible physiopathological bases of these intrafamilial phenotypic variations are discussed.** © 2008 Movement Disorder Society

Key words: aceruloplasminemia; ceruloplasmin; deferoxamine; iron; therapy.

Hereditary aceruloplasminemia (HA) is a rare autosomal recessive disease characterized by iron overload and progressive neurodegeneration.[1] The disease is caused by the absence of serum ceruloplasmin (CP), a copper-containing ferroxidase, which catalyzes the oxidation of ferrous to ferric iron, a change required for the normal transportation of iron by plasma transferrin. Ceruloplasmin, therefore, plays a crucial role in the metabolism of iron and participates in its mobilization from tissue stores.[2]

In HA iron accumulates in several organs, including the liver and pancreas, but brain involvement predominates, and the presentation almost invariably involves neurologic abnormalities (retinal degeneration, movement disorders, ataxia, and dementia).[1,3] Moreover, diabetes mellitus and a mild-to-moderate degree of sideropenic anemia with elevated serum ferritin are constant features which often precede the nervous system involvement.[4]

We report the case of two Italian HA siblings, native of Sardinia, carrying the same novel mutation in the *CP* gene but presenting with markedly different phenotypes.

CASE REPORT

Case 1

The proband is a 56-year-old man, admitted to our hospital in November 2004, 8 years after the onset of progressive neurological and psychiatric symptoms (personality changes, gait impairment, and bradykinesia). These symptoms had worsened rapidly in the course of the few months preceding admission. Progressive cognitive impairment and behavioral disorder

This article includes supplementary video clips, available online at http://www.interscience.wiley.com/jpages/0885-3185/suppmat.

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