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Two Cases of Benign Monomelic Amyotrophy of the Lower Extremities

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- Abstract -

Benign monomelic amyotrophy(BMA) is an uncommon cause of progressive mildly disabling atrophy and weakness of a limb. It predominantly affects the distal upper limb of young men. I present two men with BMA of the lower extremities. Although the disorder seemed clinically confined to a arm or leg, I confirmed by electromyography evidence of denervation in the other extremities. I reviewed the literatures and discuss the differential diagnosis. BMA is a diagnosis of exclusion that requires consideration in men with unilateral arm or leg atrophy and weakness.

Key Words : Benign monomelic amyotrophy

BMA is a rare disorder causing atrophy of an extremity, usually in young men. Upper extremity involvement is most frequent. I describe two men whom diagnosed as BMA of the lower extremities after an extensive work-up.

CASE REPORTS

Case No. 1

A 45-year-old man was first noted to have painless slowly progressive atrophy limited to the left lower leg 4 years ago. He did not have cramps or fasciculations. There was no history of poliomyelitis, trauma, or radiation treatment except hypertension for 6 months. Family histo-

ry was negative for neuromuscular disease. Examination at 45 years of age revealed atrophy of the tabialis anterior and gastrocnemius muscles and mild atrophy of the left foot muscles. Strength was decreased to 4.5/5 in the left tibialis anterior and 4/5 in the gastrocnemius muscles. Reflexes was normal except for an absent ankle jerk. Sensation was intact. Straight leg rasing test is normal in both legs. He has a mild difficulty in toe walking of the left leg. During first 1.5 years after his first symptom, the symptom was progress rapidly but afterthen that was stationary or mild progressive state for 2.5 years.

Magnetic resonance imaging(MRI) of the lumbosacral spine revealed a mild disc bulge with posteriorly projecting osteophytes at L4-5 and

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L5-S1 interspaces. Routine laboratory studies, thyroid function tests, a collagen vascular screen, B12 and folate levels, serum protein electrophoresis and immunofixation, anti-GM1 antibodies, and hexosaminidase A level were normal.

Motor (median, ulnar, peroneal, and tibial) and sensory (median, ulnar, and sural) nerve conduction studies of the upper and lower extremities were normal, including F-waves. But H-reflex was absent in left leg. Electromyography (EMG) showed positive sharp waves and fibrillations in the bilateral medial gastrocnemius muscles. Left middle and lower lumbar paraspinal muscles had positive sharp waves. And giant motor unit potentials (MUP) were present in right tibialis anterior muscle. But fasciculations were absent in all extremities and lumbosacral paraspinal muscles. The interference pattern was reduced in the left medial gastrocnemius and tibialis anterior muscles.

Muscle biopsy of the left gastrocnemius muscle revealed chronic neurogenic changes.

Case No. 2

A 16-year-old boy was first noted to have painless slowly progressive atrophy limited to the left lower leg more than 2 years ago. He did not have cramps and fasciculations. There was no history of poliomyelitis, trauma, or radiation treatment. Family history was negative for neuromuscular disease except his father had poliomyelitis from 8 months old. Examination revealed atrophy of left gastrocnemius muscle. Strength was decreased to 4.5/5 in the left gastrocnemius muscle. Reflexes and sensation were normal. Straight leg raising test is normal in both legs. He did not have a difficulty in toe and heel walking of the left leg. During 2 years after his first symptom, the symptom was progress very slowly.

MRI of the whole spine revealed a normal findings. Routine laboratory studies, thyroid function test, a collagen vascular screen, B12 and folate levels, serum protein electrophoresis and immunofixation, anti-GM1 antibodies, and hexosaminidase A level were normal.

Motor (median, ulnar, peroneal, tibial) and sensory (median, ulnar, and sural) nerve conduction studies were normal, including H-reflexes and F-waves. EMG showed positive sharp waves in the right biceps brachii and left vastus lateralis muscles. Right middle cervical paraspinal muscles had positive sharp waves. And left vastus lateralis muscle had fasciculations. Giant MUPs were present in right first dorsal interossei, bilateral tibialis anterior, gastrocnemius, and vastus lateralis muscles. The interference pattern was reduced in the upper and lower extremity muscles.

Muscle biopsy of the left gastrocnemius revealed chronic neurogenic changes.

DISCUSSION

Motor neuron disease often begins in a focal area in one extremity, and in most cases, the disease spreads steadily and rapidly from one limb to another¹. In contrast, BMAs are rare conditions in which neurogenic atrophy is restricted either to the upper or lower limb. BMAs are usually sporadic, have insidious onset and slow progression followed by stabilization, are clinically confined for many years to a single limb and lack of sensory, bulbar, and pyramidal signs².

Many terms have been coined to describe this condition (Table 1)³⁻⁵.

BMAs, which was originally described as juvenile muscular atrophy of the distal upper extremity by Hirayama et al., in Japan in 1959, affects only a limited number of myotome⁶. In 1981, Prabhakar et al⁷. reported 40 cases of wasted leg syndrome and they suggested that those cases were clinically different from other anterior horn cell disorders. In 1984, Riggs et al⁸. reported unilateral amyotrophy of lower limb which was clinically benign and focal. Uncini et al⁴. named this disorder as benign monomelic amyotrophy of lower limb. Thereafter numerous cases with asymmetrical or even unilateral muscular atrophy restricted to the upper and more rarely lower limb have been reported mainly from Japan, Malaysia, and India. But amyotrophy confined for long time to the

Table 1. *Monomelic amyotrophy synonyms*⁵

Monomelic atrophy
Benign focal atrophy
Benign focal amyotrophy
Benign monomelic amyotrophy
Distal amyotrophy of predominantly the upper limbs
Juvenile segmental muscular atrophy
Juvenile type of distal and segmental atrophy of upper extremities
Juvenile muscular atrophy of the upper extremity
Juvenile nonprogressive muscular atrophy localized in hand and forearm
Juvenile distal spinal muscular atrophy of upper extremities
Juvenile amyotrophy of distal upper extremity
Non-familial spinal segmental muscular atrophy in juvenile and young subjects
Non-familial juvenile distal spinal muscular atrophy of upper extremity
Non-familial juvenile central neurogenic muscular atrophy
Focal cervical poliopathy causing juvenile muscular atrophy of distal upper extremity
Monomelic spinal muscular atrophy
Benign juvenile focal muscular atrophy of upper extremities
Spinal monomelic amyotrophy
Unilateral juvenile muscular atrophy of upper limbs

lower limb have been reported rarely from western countries^{8,11}.

The distinct etiopathogenesis of BMAs has not been identified. But Uncini et al⁴. and Di Muzio et al⁹. suspected disturbances of the motor neurons in the anterior horn at L4-S2 and considered the disease a clinical variant of spinal muscular atrophy. Riggs et al⁸. also suggested that BMAs may be a variant of chronic spinal muscular atrophy. But Gourie-Devi et al¹². suggested that monomelic amyotrophy differs from spinal muscular atrophy in not being familial and having atrophy virtually confined to the muscles of one limb. In the non progressive form of spinal muscular atrophy of distal upper limb, Hirayama et al.¹³ proposed cascade of pathogenetic events as: (1) forward displacement of the posterior wall of the dural canal during repeated neck flexion, (2) lower cervical spinal cord compression, (3) chronic microcirculatory disturbances in the territory of the anterior spinal artery resulting in necrosis of the anterior horns which are more vulnerable to ischemia. A similar pathogenetic mechanism seems unlikely because lumbosacral cord is at the level of T10-L1 segments where the spine is quite rigid⁸.

Another possibility is that BMAs might be the sequela of an undiagnosed or subclinical poliomyelitis in infancy. However more evidence is needed to confirmed the hypothesis that motor neuron disease and particular monomelic amyotrophy might be a late consequence of subclinical poliovirus infection⁹. And others and my patients does not have previous poliomyelitis.

And a recent genetic study revealed that the gene for survival of motor neuron has been deleted in proximal spinal muscular atrophy^{14,15}. But Di Guglielmo et al². reported that deletion at the survival motor neuron gene locus are not present in BMAs of upper and lower limb and suggested that these disorders are not only clinically but also genetically separate entities from proximal spinal muscular atrophies.

Baruah and Baruah¹⁶ studied the patients of focal leg muscle atrophy with fatty infiltration and myopathic changes in a clinical setup of lumbar canal stenosis due to disc herniation. They suggested the muscular atrophy may be due to focal myopathy that may have been aggravated by proximal neural pathology (lumbar canal stenosis).

The cardinal features of BMAs were sporadic occurrence, insidious onset in the second and third decades, male predominance, slow progression followed by a stabilization and is clinically limited, for at least 3 years, to one lower limb with no cranial nerves, sensory, pyramidal or bulbar signs and normal nerve conduction^{4,9,12,17}.

Case number 2 of my patients was a little short duration of disease than other cases, but other clinical findings were same as above mentioned features.

And other criteria helpful in differential diagnosis are disproportion between hypotrophy and disability and a selective, prevalent, asymmetrical involvement of leg posterior muscles and of caput longus of biceps femoris muscle by CT⁹.

There are no specific laboratory tests for BMAs. Creatine kinase level and cerebrospinal fluid examination are normal. In a few cases, levels of anti-GM1 antibodies may be slightly to moderately elevated. When these antibodies are elevated, careful electrodiagnostic tests should be performed to investigate possible multifocal

conduction blocks¹. My cases also did not show any specific laboratory abnormalities.

On neurophysiological testing, patients usually have normal nerve conduction studies. But some patients exhibit only slight abnormalities manifested by reduced compound motor action potentials. There is no evidence of conduction block. And in one-third of cases, sensory nerve conduction studies are slightly abnormal^{1,11}. Fibrillation and fasciculation potentials in variable numbers of muscles are found on EMG in the majority of cases. Chronic neurogenic motor unit changes are prominent, with decreased numbers of motor units firing at a rapid rate. The C5-T1 myotomes are most commonly involved when the arms are affected. The electrodiagnostic features are the same as those seen in motor neuron disease. The involvement, when which appears to be unilateral clinically in 70% of cases, often turns out to be bilateral on the basis of EMG studies¹. And two-third of western patients showed chronic denervation in unaffected limbs, suggesting more diffuse subclinical anterior horn cell involvement¹¹. My patients also showed chronic denervation in unaffected limbs, suggesting more diffuse subclinical anterior horn cell involvement.

It seems that there is a precise sequence of muscle involvement related to disease duration. At the beginning the caput medialis of gastrocnemius is involved, followed by the caput lateralis and soleus and only later by tibialis anterior and the other muscles of anterior compartment. In the thigh the first muscle to be affected is the caput longus of biceps femoralis, followed by semitendinosus, semimembranosus and rectus femoris⁹.

Pathologically, biceps muscle biopsies revealed chronic neurogenic changes in two of three patients⁹. This evidence highlights subclinical arm muscle involvement in BMAs of the leg. In affected muscles, typical findings include atrophic angulated fibers and prominent endomysial connective tissue. In unaffected limbs, mild fiber type grouping is frequently found¹¹. My patients also showed chronic neurogenic changes as seen in other BMAs.

The differential diagnosis for lower extremity monomelic amyotrophy includes radiculopathy,

plexopathy, post-polio syndrome, multifocal motor neuropathy, a distal form of spinal muscular atrophy, and motor neuron disease^{1,5,11}. Among them, most important differential diagnosis of BMAs are motor neuron disease. Widespread fibrillations and fasciculations on EMG, upper motor neuron involvement, and the progressive nature of amyotrophic lateral sclerosis (ALS) help differentiate it from BMAs¹. Of particular importance is the state of the reflexes. In BMAs reflexes are always absent or diminished, whereas in classical ALS, the reflexes are always abnormally brisk, despite atrophied and weak muscles. In those patients with focal weakness and brisk reflexes in one extremity, despite a stable clinical course for a year or two, the disease invariably spreads to other extremities, becoming ALS. In those on the other hand, with diminished or absent reflexes in a weak limb, the disease remained focal, confirming the diagnosis of BMAs¹. However, recent-onset monomelic amyotrophy cannot be separated definitely from ALS without several years of follow up. Not only does clinical weakness usually spread to another limb within 3 years of onset, most patients with ALS do not survive beyond 5 years^{9,11}. Di Muzio et al⁹. suggest muscular CT showing a selective and characteristic pattern might be helpful to diagnose BMAs even in the early stages and indicates a favorable prognosis. And Hamano et al¹⁰. suggested that muscle MRI is very useful for detecting affected muscles, especially deep skeletal muscles in patients with monomelic amyotrophy of lower limb.

In the context of slowly progressive focal weakness, multifocal motor neuropathy may resemble BMAs. Some patients with a diagnosis of BMAs have had moderately elevated anti-GM1 antibodies, although conduction blocks were absent. These patients have been treated with intravenous immunoglobulin, but without benefit¹.

Although BMAs progress slowly, it may seriously impair the involved extremities. Physical and occupational therapy help maintain function. Appropriate splinting and bracing are essential. In some patients with focal weakness in a group of muscles whose function is crucial for certain activities, tendon transfer using spared muscle tendons can be considered¹.

In summary, it is important to bear in mind

that BMAs may mimic more serious diseases as motor neuron disease. So, timely recognition, close follow-up, and exclusion of other diseases should be coupled with reassuring the patient that the disorder will stabilize and not lead to significant disability. The etiopathogenesis of this sporadic electromyographically generalized anterior horn cell disease with asymmetric focal clinical expression, strong male predominance, and striking geographic difference remains completely unexplained.

1. Mitsumoto H, Cwik VA, Neville HE, Pestronk A, Shields R. Benign focal amyotrophy. *Continuum* 1997;3:111-115.
2. Di Guglielmo G, Brashe C, Di Muzio A, Uncini A. Benign monomelic amyotrophies of upper and lower limb are not associated to deletions of survival motor neurons gene. *J Neurol Sci* 1996;141:111-113.
3. Serratrice G. Spinal monomelic amyotrophy. In: Rowland LP. *Advances in neurology*. Vol.56. New York:Raven Press. 1991; 169-173.
4. Uncini A, Servidei S, Delli Pizzi C, Cutarella R, Di Muzio A, Gambi D, et al. Benign monomelic amyotrophy of lower limb: report of three cases. *Acta Neurol Scand* 1992;85:397-400.
5. Donofrio PD. Monomelic amyotrophy. *Muscle Nerve* 1994; 17:1129-1134.
6. Hirayama K, Toyokura Y, Tsubaki T. Juvenile muscular atrophy of unilateral upper extremity: a new clinical entity. *Psychiatric Neurol JPN* 1959;61:2190-2197.
7. Prabhakar S, Chopra JS, Banerjee AK, Rana PVS. Wasted leg syndrome: a clinical, electrophysiological and histopathological study. *Clin Neurol Neurosurg* 1981;83-1:19-28.
8. Riggs JE, Schochet SS, Jr, Gutmann L. Benign focal amyotrophy. *Arch Neurol* 1984;41:678-679.
9. Di Muzio A, Delli Pizzi C, Lugaesi A, Ragno M, Uncini M. Benign monomelic amyotrophy of lower limb: a rare entity with a characteristic muscular CT. *J Neurol Sci* 1994;126:153-161.
10. Hamano T, Mutoh T, Hirayama M, Ito K, Kimura M, Aita T, et al. MRI findings of benign monomelic amyotrophy of lower limb. *J Neurol Sci* 1999;165:184-187.
11. Mimachkie MM, Justiz W, Vriesendorp FJ. Benign monomelic amyotrophy of the lower extremity: report of two cases and literature review. *J Clinical Neuromuscular Disease* 2000;1:181-185.
12. Gourie-Devi M, Suresh TG, Shankar SK. Monomelic amyotrophy. *Arch Neurol* 1984;41:388-394.
13. Hirayama K, Tomonaga M, Kitano K, Yamada T, Kojima S, Arai K. Focal cervical poliopathy causing juvenile muscular atrophy of distal upper extremity: a pathological study. *J Neurol Neurosurg Psy* 1987;50:285-290.
14. Brahe C, Servidei S, Zappata S, Ricci E, Tonali P, Neri G. Genetic homogeneity between childhood-onset and adult-onset autosomal recessive spinal muscular atrophy. *Lancet* 1995; 346:741-742.
15. Lefebvre S, Burglen L, Reboullet S, Clermont O, Bulet P, Cruaud C, et al. Identification and characterization of a spinal muscular atrophy-determining gene. *Cell* 1995;80:155-165.
16. Baruah JK, Baruah GR. Monomelic leg atrophy: spinal stenosis or a focal myopathy? *Muscle Nerve* 2000;23:1638.
17. de Visser M, Ongerboer BW, Verbeeten B, Jr. Electromyographic and computed tomographic findings in five patients with monomelic spinal muscular atrophy. *Eur Neurol* 1988; 28:135-138.