

Effect of Levetiracetam on Truncal Tic in Neuroacanthocytosis

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Abstract- We report on an uncommon manifestation of neuroacanthocytosis in a 31-year-old woman and the successful use of levetiracetam in the treatment of her neurological symptoms. Truncal tic is one of the major presenting features of this patient. We find that Levetiracetam, a new antiepileptic drug, was effective in eliminating this patient's truncal jerks and motor tic manifestations, such as eyelid blinking and head nodding. Levetiracetam can therefore be considered as a choice for the symptomatic therapy in neuroacanthocytosis.

Key Words: Levetiracetam, Neuroacanthocytosis, Truncal tic

Acta Neurol Taiwan 2006;15:38-42

INTRODUCTION

Neuroacanthocytosis is an autosomal recessive movement disorder caused by mutation in CHAH gene on chromosome 9q21⁽¹⁾ but sporadic cases have been reported⁽²⁾. The exact mechanism of the pathologic changes is still unknown. There are usually atrophy and neuronal loss within structures of basal ganglion, particularly within the caudate nuclei, the putamen, and the globus pallidus^(3,4). In addition, the disorder may be confirmed by demonstrating that acanthocytes account for over 3% of the peripheral RBCs⁽²⁾. The classic features of neuroacanthocytosis includes chorea, orofaciolingual dyskinesia, tic, dysarthria, areflexia, seizure, peripheral neuropathy with areflexia, parkinsonism, elevated creatine kinase level, and dementia^(2,3). We describe a patient with neuroacanthocytosis and successful treatment of

her repetitive motor tics of head, neck and trunk with levetiracetam.

CASE REPORT

A 31-year-old woman presented with a 2-year history of gradually progressive involuntary movement. Her disease started insidiously with easy drooling and sizzling. One year before admission to the hospital, she began to experience orolingual movement with self-mutilation of the lips and tongue, slurred speech, rapid eyelid blinking and head shaking. There are internal impulses to protrude her tongue and blink her eyelid, and this impulses could only be suppressed transiently. Her gait was disturbed by intermittent axial jerk, which could also be suppressed transiently. Her cognitive ability remained normal. There was no organomegaly or

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Received April 27, 2005. Revised May 25, 2005.

Accepted October 25, 2005.

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steatorrhea. Family history showed that no member is affected by any neurological disorders. The patient was not married and had no children. At first she was treated with oxazolam (10mg t.i.d.), which partially suppressed the tics. However, the above neurological symptom aggravated again and she was admitted for further management.

Physical examination was unremarkable, except for a wound at the lower lip and buccal mucosa. Neurological examination showed normal mental status. No Kayser-Fleischer ring was found in the cornea. Vertical and horizontal pursuits and saccades were normal. Rapid eyelid blinking, moderate drooling, orolingual dyskinesia with involuntary tongue and lip biting, and intermittent head nodding jerks were observed. She had difficulty in opening her mouth fully and moving her tongue smoothly. Sometimes her tongue pushed food out of the mouth instead of swallowing down, although the swallowing function was normal and she was not malnourished. There was not bradykinesia nor rigidity. Muscle power was normal. Neither muscle wasting nor fasciculation was observed. Cerebellar function and sensation were normal. Deep tendon reflexes showed generalized areflexia with flexor-type plantar responses. Her posture was mildly stooping and her gait was impaired by intermittent truncal tic movement and paroxysmal forceful anteflexion, which can only be partly and transiently suppressed.

Routine blood test results were normal except mild elevation of serum creatine kinase 321 IU/L (normal range 22~269 IU/L). Copper, ceruloplasmin, vitamin E (9.8 µg/ml levels (normal range 5.5~17 µg/ml), lipoprotein, antinuclear antibody, lipid profile and thyroid hormone were normal. Numerous acanthocytes (49%; Fig. 1) were present on a peripheral blood smear by central laboratory and were demonstrated by scanning electron microscope (Fig. 2). Electrocardiogram and chest radiograph were normal. Radiographic studies of the thoracic and lumbar spines showed scoliosis. Neuropsychological examination showed normal cognitive function. Electromyography of her extremities showed axonal polyneuropathy. There was no evidence of epileptogenicity on electroencephalography.

Computed tomography and magnetic resonance imaging scan of the brain showed ventricular dilatation with atrophy of the caudate nucleus bilaterally (Fig. 3). Surface electromyogram (EMG) showed episodes of involuntary muscle contraction, each lasting for over 100ms (Fig. 4).

She was treated with piracetam (4800 mg b.i.d.) initially and then titrated to a larger dose (4800 mg q.i.d.). Propranolol (10 mg t.i.d.) and clonidine (0.075 mg b.i.d.) were also administered to treat her inner impulse. Because

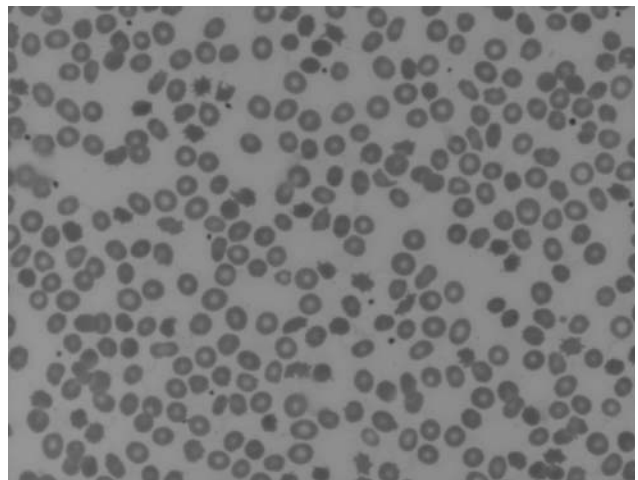


Figure 1. Liu stain of peripheral blood smear showed significant acanthocytosis (magnification $\times 40$).

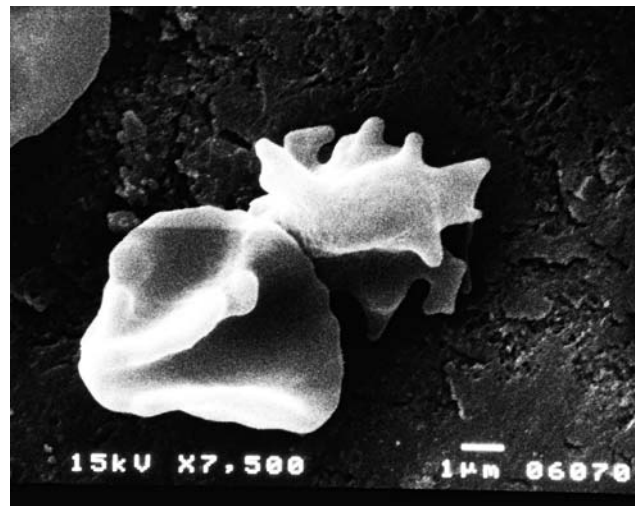


Figure 2. Scanning electron microscopic illustration of the acanthocyte (magnification $\times 7500$).

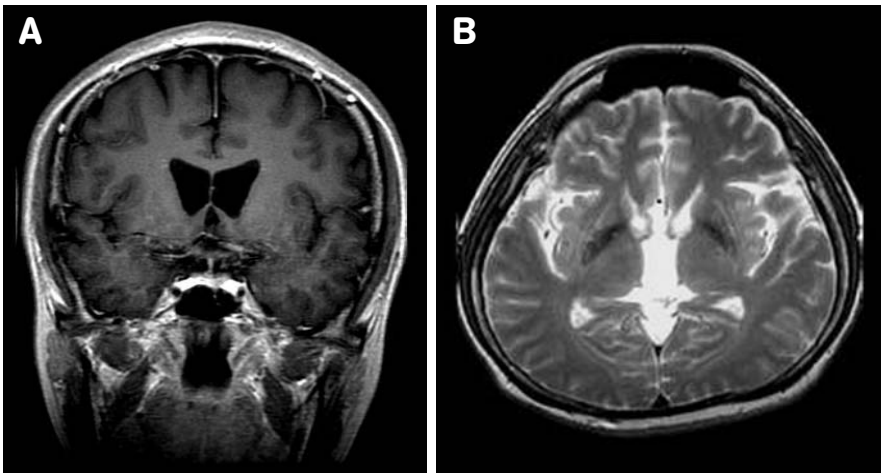


Figure 3. (A) T1 Flair magnetic resonance image with contrast (repetition time: 1753.11, echo time: 9.248), coronal section. (B) T2-weighted magnetic resonance image (repetition time: 4000, echo time: 101.088), axial section. Magnetic resonance images of the brain showed atrophy of bilateral caudate nuclei, putamens, and globus pallidus, with dilatation of the anterior horns of the lateral ventricles.

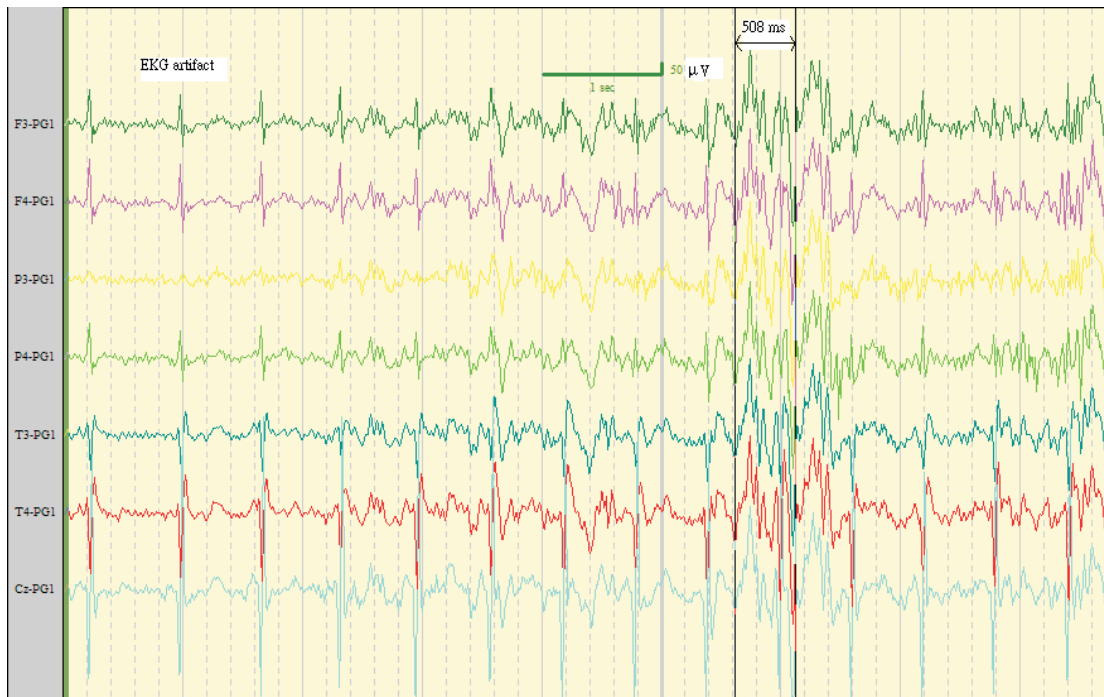


Figure 4. Multichannel surface EMG recording from sternocleidomastoid, pectoralis major, and paraspinal muscles showed discharges lasting for ~508 ms. (rate: 10 sec/page, sens: $50\mu\text{V}/\text{min}$, low filter: 0.1Hz, high filter: 100Hz)

the truncal tic and the other repetitive motor tics were only partially suppressed, we switched piracetam to lev-
etiracetam (250mg twice a day). The truncal and multi-
ple focal tics were then suppressed completely.

DISCUSSION

We describe a patient with adult onset of oro-lingual
dyskinesia, eyelid tic, and intermittent rapid ante-
flexion of her trunk (truncal tic). The finding of numerous acan-

thocytes (49%) in the peripheral blood smear provided the major basis for the diagnosis of neuroacanthocytosis. There are many different syndromes with neurological dysfunction and red cell acanthocytosis, including chorea-acanthocytosis, Mcleod syndrome, panthotenate kinase associated neurodegeneration, abetalipoproteinemia, Anderson disease, severe malnutrition, thyroid disorders, and liver cirrhosis⁽⁵⁾. Our investigation clearly ruled out malnutrition, thyroid disorder, liver cirrhosis. At this point the most important differential diagnosis that should be considered in this case is Huntington's chorea (HC). HC has many features in common with neuroacanthocytosis, such as the age of onset, chorea, tics, personality changes and caudate atrophy on neuroimage^(6,7). However, lip and tongue biting, absent or diminished tendon reflexes, vocalization and absence of family history all help to exclude the diagnosis of HC. The diagnosis of neuroacanthocytosis in this patient is thus established by the clinical neurological symptoms, negative family history and biochemical data, acanthocytes in peripheral blood smear, and brain image findings..

Clinical manifestations of neuroacanthocytosis include characteristic orofacial dyskinesia (tongue protrusion and lip biting), dysphagia, dysarthria or vocalization, movement disorder (parkinsonism, tics, chorea, dystonia), cerebellar ataxia⁽⁸⁾, frontosubcortical type of dementia, and psychiatric features^(2,9). Repetitive motor tics were present in 8 of the 19 patients reported by Hardie et al⁽²⁾. Multiple focal tics including those in the face and head were the presenting features of our patient. Tics are defined as sudden, repetitive, stereotyped motor movement or phonic production that involve discrete muscle groups⁽¹⁰⁾. They are characterized by irresistibility but can be suppressed temporarily by willpower and are relatively easy to imitate. Tics most often affect muscles in the face and head⁽¹¹⁾; and truncal tics are relatively rare. Another feature in our patient is the jerky movement of her trunk.

The truncal jerks interfered with her gait, and could be suppressed by her willpower transiently. The truncal jerks are therefore considered as a presenting feature of tics. However, due to the sudden, brief, and shock-like component of the jerk, the possibility of myoclonus

should also be considered and the differential diagnosis could be made based on surface electromyographic findings. Myoclonus appears as a highly synchronous discharges of multiple motor units and stands out of the background on EMG recordings. The duration of the myoclonus EMG discharge is most commonly 100ms or less⁽¹²⁾. Because the duration of EMG discharges was significantly longer than 100ms in our patient; the truncal jerks we observed most likely should be tic in origin.

The basal ganglia have been regarded as a probable substrate for the generation of tics. The pathophysiological basis may be related to abnormalities in inhibitory neurotransmission (γ -Aminobutyric acid, GABA)⁽¹³⁾. Tourette syndrome is the most severe form of tic disorder, for which modification in the activity of GABAergic system indeed shows beneficial effects. The treatment for neuroacanthocytosis is symptomatic. The symptom of parkinsonism in neuroacanthocytosis may respond to dopaminomimetic therapy⁽¹⁴⁾, but the responses of the involuntary movements are generally poor. The traditional medications for the treatment of tics include haloperidol, pimozide, fluphenazine, and clonidine, all of which may have considerable side effect. In view of the possible role of GABA in the dysfunction of the basal ganglion in patients with Tourette syndrome^(11,15), GABAergic drugs such as baclofen and clonazepam may constitute another option to treat tics. Levetiracetam is a new and effective antiepileptic drug and has been approved as adjunctive therapy for partial seizure in adults⁽¹⁶⁾. Levetiracetam has also been used in the treatment of movement disorders, including cortical, post-hypoxic and post-encephalitic myoclonus, dystonia, paroxysmal kinesio-genic choreoathetosis, and essential tremor⁽¹⁷⁻¹⁹⁾. Levetiracetam blocks the effect of negative GABA-receptor modulators and has been reported to be effective against tics⁽²⁰⁾. In this report we also documented the dramatic effect of levetiracetam in the treatment of tics in a patient with neuroacanthocytosis.

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