



Case of Neuroacanthocytosis Course With Neuropathy, Epilepsy and Choreiform Movement Disorder

CASE REPORT

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ABSTRACT

Neuroacanthocytosis is a neurodegenerative disease characterized by movement disorders, seizures, dementia, and behavioral changes, as well as spiked acanthocytes in peripheral smears, but it is rarely accompanied by axonal neuropathy. Before making a definitive diagnosis of neuroacanthocytosis, diseases like Huntington disease, Parkinson disease, Tourette syndrome, and Wilson disease should first be considered. Diagnosis is essentially based on the clinical picture and the presence of acanthocytes in peripheral blood. Its treatment is symptomatic, and therefore treatment measures may vary from case to case. Drugs such as anticholinergics, antipsychotics, and antiepileptics are typically used for the treatment of the symptoms. Chorea-acanthocytosis is an autosomal recessive, progressive disease, for which the neurological symptoms start in the 20s. The onset symptoms are generally mild cognitive or psychiatric disorders and these complaints are observed before the neurological findings appear. In some patients, epileptic seizures may occur before the movement disorders. In this article, a 38-year-old male case featuring both common and rare clinical reflections of neuroacanthocytosis is presented.

Keywords: Choreiform movement disorder, epilepsy, neuroacanthocytosis, neuropathy

INTRODUCTION

Neuroacanthocytosis covers a genetically heterogeneous group of diseases characterized by neurological findings and symptoms accompanied by spiked erythrocytes in the peripheral smear. The neurological findings of this disease include movement disorders such as chorea, dystonia, orofacial dyskinesia, tic, ataxia, cognitive inefficiency, personality changes, axonal neuropathy, and epilepsy (1). Each major type of neuroacanthocytosis syndrome has its own etiology; generally, it is reported with autosomal recessively inherited disorder. Also, autosomal dominant or x-linked recessive disorder has also been identified. The literature reports other sporadic cases as well (2, 3). For diagnosing neuroacanthocytosis syndromes, detection of acanthocytes in the peripheral blood is an important criterion; however, since the presence of acanthocytosis alone is not significant, there should be accompanying clinical findings (4). The case to be presented was selected due its unusual nature, in that it involves many common and rare clinical reflections of neuroacanthocytosis syndromes.

CASE REPORT

A 38-year-old male patient had been having epileptic seizures (generalized tonic-clonic seizure) for almost 6 years; he had undergone a cervical disk herniation surgery, and he experienced peripheral facial paralysis. For two years, he had experienced involuntary movements in his face, body, and extremities; difficulty in walking; balance and speech disorder; and all these symptoms were gradually increasing. To address the epileptic seizures, he was taking 500 mg each of valproic acid (VPA) and levetiracetam (LEV) three and two times a day, respectively. The patient was hospitalized in our clinic to explore the possibility of making a preliminary diagnosis for Wilson's disease, Huntington's disease (HD), chorea, or neuropathy. The findings during his neurological examination were as follows: he had dysarthria and choreiform movements in all four extremities, the body, and in the oromandibular region; he did not have deep tendon reflexes in lower extremities; and he had a positive Romberg finding and vibration sensation was reduced in both lower extremities. There were no abnormalities in the hemogram and biochemical tests of the patient. His sedimentation rate was normal. Patient got a creatine phosphokinase value of 650 u/L. The thyroid function tests and vitamin B12 levels were within normal ranges, and the serum VPA level was at an active level. In his cranial magnetic resonance imaging (MRI), mild ventricular dilatation, cerebral, and cerebellar atrophy were detected. No significant pathologies were detected in his spinal MRI, except for the defective appearance, which was a secondary symptom

Cite this article as:

Sönmez A, Göl, MF, Erdoğan FF. Case of Neuroacanthocytosis Course With Neuropathy, Epilepsy and Choreiform Movement Disorder. Erciyes Med J 2017; 39: 140-2.

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Submitted
26.04.2017

Accepted
05.07.2017

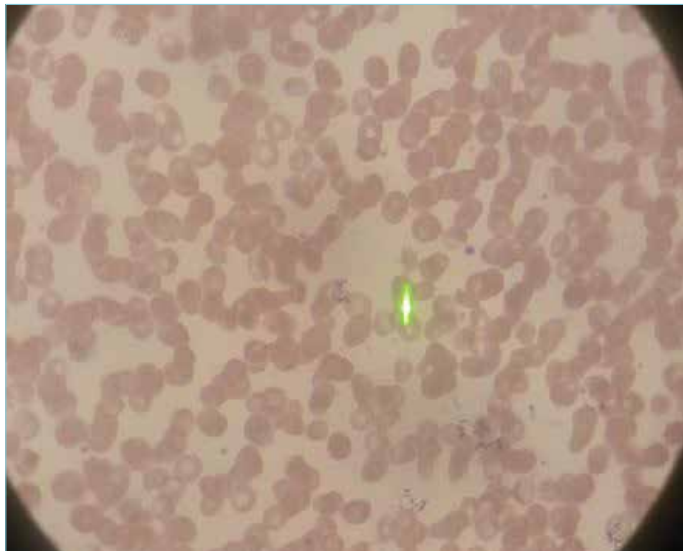
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Table 1. Comparative properties in neurodegenerative neuroacanthocytosis syndromes

Disease	Chorea -acanthocytosis	McLeod syndrome	Huntington-like disease 2	Pantothenate kinase-related neurodegeneration
Gene	VPS13A	XK	JPH3	PANK2
Protein	Chorein	XK protein	Junctophilin-3	Pantotenat kinaz 2
Heredity	Autosomal recessive	x dependent	Autosomal dominant	Autosomal recessive
Acanthocytes	+++	+++	Normal	+/-
Serum CK(U/L)	300-3000	300-3000	+/-	Normal
Neuroimaging	Sitriatal atrophy	Sitriatal atrophy	Sitriatal and Cortical atrophy	Eye of the Tiger sign
Starting age	20-30	25-60	20-40	Childhood age
Chorea	+++	+++	+++	+++
Other movement disorders	Eating and walking dystonia, Tongue and lip biting, Parkinsonism	Vocalizations	Dystonia, Parkinsonism	Dystonia, Parkinsonism, Spasticity
Seizures	Generalized and Complex partial	Generalized	No	No
Neuromuscular findings	Areflexia, Weaknes, Atrophy	Areflexia, Weaknes, Atrophy	No	No
Cardiac findings	No	Atrial fibrillation, Malignant arrhythmia, Dilate Cardiomyopathy	No	No

**Figure 1.** Approximately 50% acanthocytes were observed in the peripheral smear (Diluted with saline)

of the cervical disk herniation surgery he had undergone. Approximately 50% acanthocytes were observed in the peripheral smear (Figure-1, diluted with saline). The existing findings led us to a diagnosis of neuroacanthocytosis syndromes, as the serum copper, serum ceruloplasmin, and 24-hour urine copper levels required for the definitive diagnosis of Wilson's disease were normal. Kayser-Fleischer ring was not detected. Results from the patient's video EEG monitoring recording showed there to be no significant epileptic pathologies; there were no significant car-

diac pathologies detected in the transthoracic ECHO; and finally, there was no sural nerve response obtained in the electroneuromyography (ENMG).

The median and ulnar nerve sensorial transmission speeds were detected to be low, and the lower extremity peroneal nerve transmission speed was below the normal value. His mini mental state examination (MMSE) score was 26 of 30, which indicates mild cognitive disorder. No significant deficits were observed in frontal lobe tests. In addition to the VPA he was taking for epilepsy, the patient was prescribed 5 mg of haloperidol two times to address his involuntary movements. Because the patient's family history showed that he had a sister with epilepsy, a peripheral smear was studied for possible neuroacanthocytosis syndromes. No acanthocytes were observed in the peripheral smear. Based on the history provided by the patient, none of the other family members and relatives had similar complaints or conditions. We diagnosed chorea-acanthocytosis by considering the other clinical features of the patient who had no MRI findings of the eye of the tiger, no cardiac manifestations, no family history with CK elevations.

DISCUSSION

Neuroacanthocytosis is a rare, multi-systemic, and neurodegenerative disease. The disease may be accompanied by movement disorders such as dystonia, motor and phonic tics, generalized chorea and stereotype, and/or manifest as polyneuropathy (5). Common symptoms of neuroacanthocytosis include epileptic seizures, dysarthria, and cognitive and psychiatric disorders. The most important diagnosis criteria of neuroacanthocytosis is the detection of acanthocytes in the peripheral blood; however, a diagnosis based on

acanthocytes alone, without considering the clinical picture, may lead to a medical error (6, 7). Neurodegenerative neuroacanthocytosis syndrome refers to a group of multi-systemic and neurodegenerative diseases, and after Huntington disease, it is the most common cause of hereditary chorea. Chorea-acanthocytosis is a subtype of the core neuroacanthocytosis group.

Pantothenate kinase-associated neurodegeneration, unlike other neuroacanthocytosis syndromes, begins in childhood. The autosomal is inherited and CK is normal. No seizures, neuromuscular, or cardiac manifestations are observed. The typical MRI findings of the “eye of the tiger” play an important role in sign diagnosis. Huntington disease-like 2 is also autosomal dominantly inherited. CK is normal. No seizures, neuromuscular manifestations, or cardiac findings were observed. McLeod neuroacanthocytosis syndrome shows an X-linked inheritance pattern. Serum CK (u/L) is between 300 and 3000, and seizures and cardiac, neuromuscular findings are observed. Chorea-acanthocytosis is autosomal recessively inherited. Serum CK (U/L) is between 300 and 3000 and seizures and neuromuscular findings are observed. No cardiac findings are observed. The main differences are listed in Table 1 (taken from reference 5).

Despite the different ratios reported by various sources, it is generally accepted that the ratio of acanthocytes in the peripheral blood in neuroacanthocytosis cases is 5% of total erythrocytes (2). In our case, this ratio was detected to be approximately 50%. Considering the age of complaint onset, absence of any known cardiac involvement, absence of similar complaints in family members, ENMG findings compliant with sensory-motor type neuropathy and accompanying areflexia, the presence of generalized tonic-clonic type seizures, our case was determined to indicate chorea-acanthocytosis, which is a neurodegenerative neuroacanthocytosis subgroup.

The onset symptoms are generally mild cognitive or psychiatric disorders and these complaints are observed before the neurological findings appear. In some patients, epileptic seizures may occur before the movement disorders (8). In our case, epileptic generalized tonic-clonic seizures began before the involuntary movements. During the course of the disease, findings such as characteristic phenotype chorea, orofacial dyskinesia, involuntary vocalizations, dysarthria, and dystonia are accompanying symptoms in many patients. In most of the patients with chorea-acanthocytosis, chorea-type movement disorders, orofacial lingual dyskinesia, and limb dystonia are commonly observed, whereas parkinsonism findings are rather rare. As in our case, at least in one-third of the patients, generalized-type epileptic seizures may be the first finding of the disease. Impairment in memory and coordination functions are a common, but not essential, finding. In our case, we observed a slight decrease compared with normal values in attention, motor speed and coordination functions in the frontal lobe tests conduct-

ed on the patient, and the MMSE score indicated mild cognitive disorder. Psychiatric findings are frequently seen and mostly occur in the form of psychosis, like schizophrenia or obsessive compulsive disorder. Clinical neuromuscular findings include areflexia, sensory-motor type neuropathy, weakness and muscular atrophy, whereas myopathic findings are rare in muscle biopsy and ENMG (9, 10). These findings were coherent with the ENMG and neurological examination results in our case. This case reveals the fact that neuroacanthocytosis syndromes should be considered in differential diagnosis in patients applying with seizure and choreiform movement disorder.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Conceived and designed the experiments or case: AS., MFG., FFE. Performed the experiments or case: AS., MFG., FFE. Analyzed the data: AS., MFG., FFE. Wrote the paper: AS., MFG. All authors have read and approved the final manuscript.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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