An Interesting Case of a Movement Disorder

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Abstract

Neuroacanthocytosis is a genetic neurodegenerative disorder with syndromes of variable inheritance. These hyperkinetic movement disorders are reported to be very rare. It is associated with choreiform movements, orofacial and lingual dyskinesias and acanthocytes on peripheral smear and normolipoproteinemia. Here we present a similar case.

Case Report

A 38 year old male presented with insidious onset progressive involuntary movements for past ten months (Figure 1). He had irregular semipurposeful movements of limbs, flexion extension movements of neck, facial and oral movements, lip biting and tongue biting and unsteadiness while walking progressing to generalised choreoathetosis, orofacial dyskinesia, feeding dystonia, and lip biting. Over the last six months he developed truncal and gait ataxia. These involuntary movements disappeared during sleep. There was no history of behavioural changes like psychosis or obsessive compulsive neurosis. His cognition was normal with Mini Mental Status Examination score of 27 out of 30. No history suggestive of rheumatic fever, intake of anti-psychotic or anti-epileptic drugs was elicited.

Patient was born of a non-consanguineous marriage and had six siblings. Eldest brother was treated as a case of Parkinson’s disease and he was no more. Second brother was diagnosed to be a case of seizure disorder. His younger sister too had seizure and was on antiepileptic medication. He had a son and a daughter without any history or signs of neurological disorder.

On examination patient was alert, co-operative, restless and with normal vital signs. There was no rash, muscle tenderness, muscle atrophy and skeletal deformity. Cardiovascular, respiratory system and abdomen examination were clinically normal.

On neurological examination, higher function, cranial nerve examination were normal except nasal quality of voice and occasional nasal regurgitation. Motor system examination revealed normal tone, muscle power of 4+/5 in proximal muscles of upper and lower limbs and 4/5 in distal muscles of upper and lower limbs absent biceps, triceps, supinator, knee, and ankle reflexes and bilateral flexor plantar. Sensory system examination, vibration and joint position sense were normal. Romberg sign and spurling sign were negative. Gait showed truncal instability and sudden extension movements of the trunk – rubberman gait. No fasciculation or muscle tenderness was present. Extrapyramidal system examination revealed involuntary, irregular, jerky, non-repetitive, ill-sustained, semi purposeful movements randomly distributed in character implying chorea. Orofacial dystonia or feeding dystonia, self-lip mutilation, sudden flexion and extension movement of the neck were present.

On investigation peripheral smear showed more than 30% of acanthocytes (Figure 2). EEG, ECG, ECHO, chest X ray, liver function test, renal function test, thyroid function test, serum lipids, lipid electrophoresis, serum

Fig. 1: Our patient seated with clasped hands to avoid the involuntary movement

Fig. 2: Peripheral smear of the patient showing acanthocytes

Fig. 3: Peripheral smear of elder brother showing acanthocytes

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ceruloplasmin, urinary copper, ESR, serum vitamin B 12 level, fundus examination were normal. Nerve conduction study revealed sensorimotor axonal polyneuropathy. The action potentials studied in EMG showed neuropathic changes (the motor unit potentials were of long duration, polyphasic and there was decreased recruitment). CPK level was elevated - 688 U/L. Muscle biopsy was not done since the patient was not willing. MRI brain showed normal study.

His positive family history, presence of acanthocytes in peripheral smear, normal lipids and lipoproteins, elevated creatinine kinase, peripheral neuropathy, normal Kell blood group expression, with characteristic orofacial dyskinesia, feeding dystonia, self-lip and tongue mutilation, chorea led to the diagnosis of neuroacanthocytosis. Patient was treated with anticholinergics, benzodiazepine, tetrabenazine and dopamine antagonists to control his involuntary movements and patient responded well to treatment.

On examining the peripheral smear of the patient’s second brother it was surprising to find acanthocytes confirming the genetic basis of the disease (Figure 3).

Discussion

The leading cause of adult onset chorea would be Huntington disease [HD]. Other causes of chorea include thyroid disease, lupus, drug-induced, pregnancy, stroke, and an idiopathic type. Our patient with very peculiar feature of “feeding dystonia” with tongue protrusion, orofacial dyskinesias, dysarthria, involuntary tongue and lip-biting and generalized chorea favoured the diagnosis of neuroacanthocytosis. The patient also had “rubber man” gait with truncal instability and sudden, violent trunk spasms. The presence of acanthocytes on peripheral smear proved it to be neuroacanthocytosis. The identification of acanthocytosis in peripheral blood smears may be negative in a standard setting and a negative screen does not rule out neuroacanthocytosis syndrome. A more sensitive and specific method for detecting acanthocytes uses a 1:1 dilution with physiological saline and phase contrast microscopy.

Neuroacanthocytosis (NA) syndromes were known previously under the eponym “Levine-Critchley syndrome”. In 1991, Hardie and colleagues studied a series of 19 NA patients, which for years was the pioneering work on NA. However, with recognition of the molecular genetics of the different NA syndromes, this case series turned out to be heterogeneous, including patients with Chorea acanthocytosis (ChAc), MeLeod syndrome (MLS) and Pantothenate Kinase - Associated Neurodegeneration (PKAN).

The “core” NA syndromes are - autosomal recessive ChAc caused by mutations of the VPS13A gene, and X-linked MLS, caused by mutations of the XK gene. There are several other genetic disorders in which acanthocytosis is occasionally seen, such as PKAN and Huntington disease - like 2 (HDL2). Occasional cases are reported where acanthocytes are present in other extrapyramidal features, such as paroxysmal dyskinesias or mitochondrial disease.

ChAc is a progressive autosomal recessive neurodegenerative disease with onset of neurological symptoms usually in the second decade, thus representing a late onset for an autosomal recessive disorder. The initial presentation may be subtle cognitive or psychiatric symptoms, and in retrospect patients might have related psychiatric complaints several years before the neurological symptoms. Administration of neuroleptics for psychiatric disease may confound the scenario to a neurodegenerative process. In some cases, seizures may precede the appearance of involuntary movements by as much as a decade. Most develop generalized chorea and a minority develops Parkinsonism. In addition to orofaciolingual dystonia, limb dystonia is also common. In at least one third of cases, seizures typically generalized, are the first manifestation. Memory disturbances and cognitive impairment is frequent, although not invariable. Most ChAc patients have elevated levels of creatine phosphokinase (CK). In contrast to MLS, myopathy and axonal neuropathy are usually mild. Clinical neuromuscular manifestations include areflexia, sensorimotor neuropathy, and variable weakness and atrophy. Muscle biopsy and electromyography commonly demonstrate neuropathic changes and rarely myopathic alterations. Disease usually slowly progresses over 15-30 years, but sudden death, presumably caused by seizures or autonomic involvement, may occur.

The differential diagnosis of NA syndromes depends upon the presenting symptoms, which can be protean. Initial symptoms may suggest psychiatric disease, including schizophrenia, depression, obsessive - compulsive disorder, tics, Tourette’s syndrome, cognitive impairment, personality change, or may consist of parkinsonism, chorea, dystonia, peripheral neuropathy, myopathy, cardiomyopathy, or seizures. Persons harboring the McLeod blood group phenotype are sometimes identified upon blood donation, many years or even decades prior to development of neurological symptoms. Both MLS and ChAc may be detected incidentally by the elevation of CK or liver enzymes. Recognition of the syndrome may avoid the need for invasive and non - diagnostic tests such as muscle, bone marrow, or liver biopsy. ChAc, MLS, and HDL2 all present in young to middle adulthood, but MLS has usually the latest onset of neurological symptoms. Presence of self – mutilating lip and tongue biting, or other self - mutilation such as head – scratching or finger – biting is strongly suggestive of ChAc.

So far no curative or disease – modifying treatments are available and management of the NA disorders is purely symptomatic. Recognition of treatable complications such as seizures, swallowing problems, and heart involvement is essential. Neuropsychiatric issues, particularly depression, can have a major impact upon quality of life, and these symptoms may be more amenable to pharmacotherapy than others. Dopamine antagonists or depletors such as tiapride, clozapine or tetrabenazine may ameliorate the hyperkinetic movement disorders. Anticonvulsants may have the benefit of multiple parallel effects upon involuntary movements, psychiatric symptoms, and seizures.

Non - medical therapies with a multidisciplinary approach are often helpful.

Conclusion

This case illustrates that it is
worthy to have a clinical approach to a movement disorder, carefully ruling out the causes with simpler investigations done to diagnose a major disease like neuroacanthocytosis. Neuroacanthocytosis is to be considered as a differential diagnosis in adult onset chorea with classical presentations like orofacial dyskinesias, feeding dystonia, flexion and extension dystonia of neck, self-lip mutilation etc.

References