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Idiopathic Neuroacantocytosis is a Rare Report in Iran

Abdolkarimi Babak[1], Zareifar Soheila[2], Mokhtari Maral[3]*

[1]*Department of Pediatrics, Khoramabad, Lorestan University of Medical Science*
[2]*Department of Pediatrics, Shiraz University of Medical Science*
[3]*Department of Pathology, Shiraz University of Medical Science*

[*]***Corresponding author:*** *Soheila Zareifar, Department of Pediatrics, Shiraz University of Medical Science, 7187915998, Iran, Fax +9871336332148; Tel: +98071336323731; Email: zareifars@yahoo.com; zareifars@sums.ac.ir*

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Abstract

Neuroacantocytosis is a group of genetic conditions characterized with movement disorders and acantocytosis. All these patients should be assessed for other causes of acantocytosis such as abetalipoproteinemia, Mc Leod syndrome and causes of movement disorder including Wilson disease, Huntington disease, panthotenic acid kinase deficiency, or general liver and renal disorders. Herein we present a case of idiopathic neuroacantocytosis in this paper.

Keywords: Acantocyte; Cerebral Palsy; Chorea; Neuroanatomist

Introduction

Neuroacanthocytosis is a group of genetic conditions characterized by two components of various movement disorders, neurological signs and deformation of red blood cells called acantocyte [1].

The core Neuroacantocytosis (NA) syndromes include autosomal recessive chorea-acanthocytosis and X-linked McLeod syndrome. These disorders have a Huntington disease-like phenotype of a choreatic movement disorder, psychiatric manifestations and cognitive decline, but may have additional multi-system features including myopathy and axonal neuropathy. In addition, patients with McLeod syndrome may develop a cardiomyopathy [2].

These conditions, including acanthoscytosis, chorea, McLeod syndrome, Huntington's Disease 2 (HDL2) and neurodegeneration associated with Pantothenate Kinase (PKAN) or Halervorden-Spitz, which affects the brain and extrapyramidal system as the basal ganglia.

Neurological signs include movement, posture and skeletal abnormalities, weakness, cognitive impairment, psychiatric disorders and neurodegenerative symptoms and movement disorders [3].

These diseases are hereditary, but infrequent, and in very rare cases with the scarcity of data on them. These disorders have two categories of symptoms including intermittent hemolytic attacks and progressive chronic neurologic phase.

Case Report

The patient was a 6-year-old boy admitted to the pediatric emergency department for fatigue, palor and icter.

The patient's mother stated that the child had developmental delay from childhood, but he had normal weight gain during the period of childhood. His pseudobulbar paralysis results pouring of water and food from the mouth and sometimes nasal grip while water drinking. It seems that it was artificial, repetitious, non-model, involuntary and arrhythmia, unintentional in his body, especially in the head and neck. The movement was disappeared during sleep but was not eliminated by voluntary action. Any abnormal behavior, non-direct, rough and doughy speech were not detected.

There was no history of vision disturbances, limb weakness, and cerebellar, sensory or autonomic dysfunction. He had one-time febrile convulsion at 2.5 years of age. There is no family history of neurological disorders or similar diseases.

The general physical examination the vital signs were normal. Significant bite lips according to the orofacial dyskinesia present on the inner side of the lower lip indicates repeated self-mutilation and friction of the lower lip. In physical examination the patient has sagging and rigid skeletal muscles, involuntary abnormal tongue movements, spasms of neck, mild mental retardation. On neurological examination, he was aware and oriented. Neuropsychological assessment shows slight frontal atrophy.

The memory functions assessment was normal. The behavioral changes specified in the form of repeated words and actions were continuous indicative of obsessive-compulsive behavior and anxiety. The cranial nerve examination was normal. Hypotonia reveal with a 4/5 resistance on the Medical Research Council (MRC) scale at all extremities. Generalized hyporeflexia was present without flexor plantar reflex. All primitive reflexes were absent. The examination of the sensory, autonomic and cerebellar functions was unremarkable.

The extrapyramidal system assessment showed a complex abnormal involuntary movement. Orolingual, neck, trunk and limbs were exceptional. Language was a slightly unclear form. In addition, the spectacle of head and neck alternating dystonic movements.

There were obvious feeding difficulties due to the abnormal movements of the tongue and neck.

Complete Blood Count on the Time of Admission Was:

WBC=10200 (N=45%, L=40%) / mm3, Hb=6.5 g/dl, Plt=127000 /mm3

Acanthocytosis was detected in consecutive samples of peripheral blood (Figure 1).

Echocardiography was normal. Abdominal sonography revealed mild splenomegaly, but no hepatomegaly or biliary stones.

Nerve conduction studies was not indicative of motor and sensory axonal neuropathy. Brain magnetic resonance imaging revealed caudat atrophy (Figure 2).

Kayser-Fleicher ring and retinitis pigmentosa weren't seen in ophthalmologic exam by slit lamp. Genetic study for diagnosis of Huntington's disease demonstrated 30 unstable or mutable CAG repeats. Individuals with a CAG repeat in this range will not develop HD, but there is a small possibility the CAG repeat may expand when passed from father to child and possibly

from mother to child. Further study is required before accurate diagnosis be given for this range. Although Chorea-Acantocytosis need evaluation of various mutations of a 73-exon gene on chromosome 9, VPS13A, coding for chorein. Unfortunately, it was unaccessible for us [4].

This patient was treated in adult neurology service as a case of cerebral palsy with folic acid 1 mg daily for hemolysis prophylaxis and Trihexiphenydil and Baclofen for movement disorder and muscle rigidity. He also received blood transfusion because of excessive sampling.

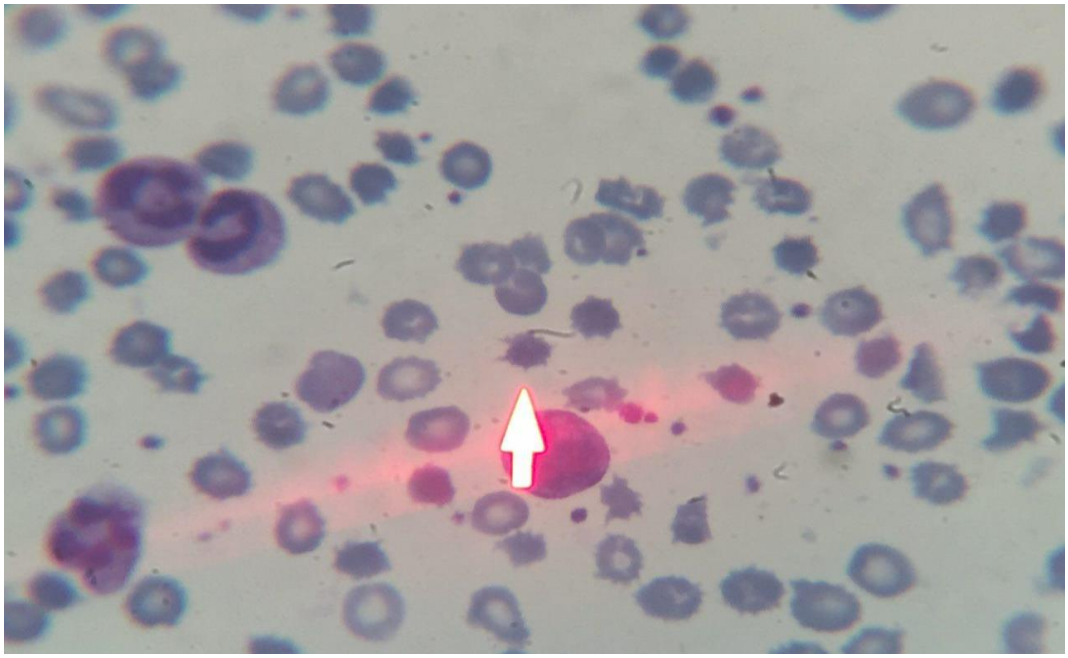

Figure 1: Peripheral blood smear, wright stain ×100, showed many acantocytes.

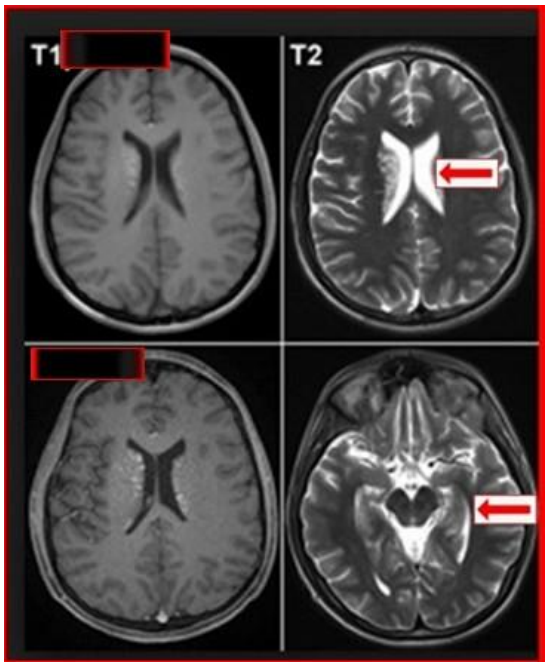

Figure 2: Brain MRI showed atrophy of the caudate.

Test	Value	Normal Range
Hb(g/dl)	6.5	
WBC/ mm^3	10200	
Platlet/mm^3	127000	
Retic count	5%	
Urine copper 24h (µg/ ml	35	Normal range: 0.3-0.8 µmol or 20-50 µg
G6PD	sufficient	
Pyrovate kinase	185	normal value is 179 ± 16 units per 100mL of red blood cells.
Urine Analysis	normal	
T.Bil	3.5	
D.Bil	1.5	
BUN	12	
Creatinine	0.4	
ceroloplasmine	3.5	Normal Values
		2.83-5.50 µmol/L or 18-35 µg/dL
Direct coombs	negative	
Indirect coombs	negative	
ANA	0.1	value less than or equal to 1:40 dilution (or < 1.0 IU) is negative.
Kell antigen on RBC	Negative	
VDRL	Negative	
C3	0.4	The normal ranges of C3 and C4 do not alter with age.
		C3 0.65 - 1.65 g/L;
C4	0.32	C4 0.16 – 0.60 g/L
CH50	350	CH50 Values % of Reference values Interpretation
		* <100 0-50 Absent or low
		* 100-300 51 to 150 Normal
		* >300 >150 High
Anti-DNA	2.4	Reference Range(s)
		≤4 IU/mL
		5-9 IU/mL
		≥10 IU/mL

Three nucleotid CAG (Huntington disease) PCR	35	Normal Values
		normal individuals (31–42 repeats
TSH	4.6	0.7 to 6.4 microunits per milliliter
T3	96	80-180 ng/dl
T4	7	4.6-12 ug/dl
TG	90	
Chol	120	
ASO	negative	
FBS	86	65-110
ALT	15	
AST	12	
ALKP	234	
LDH	365	
Tochfrol level		
Stool sudan black staining		

Table 1: patient's paraclinic parameters Prepheral blood smear revealed, increased acantocyte and dense RBC.

Discussion

Neuroacantocytosis (NA) syndrome is a rare movement disorder. The prevalence is estimated to be fewer than 1/5000000. Incidence in Iranian pediatric population is unknown. Neuroacantocytosis clinical symptoms variation change from involuntary hyperkinetic neuromuscular movements, to cognitive and behavioral changes. Beginning of symptom is usually since adulthood (>18 years old) but our patient is in late childhood period (6-12 years old) [5].

Most of the NA syndromes have an autosomal recessive inheritence while choreoacanthocytosis McLeod syndrome which one of the popular NA is, X- linked is defined by absent Kx red blood cell antigen and weak expression of Kell antigens.

In this syndrome patient has Kell minor blood group antigen. McLeod syndrome should be considered as a differential diagnosis of every choreoacanthocytosis neuromuscular disorder. Liver, spleen and cardiac involvement may be seen in McLeod syndrome. Our male patient had normal cardiac function [6]. and negative Kell antigen phenotype on his RBC.

Other NA syndromes include the neuroacanthocytosis following lipoprotein disorders such Abetalipoproteinemia or Bassen Kornzweig disease1 that body can't create lipoproteins. This defect causes fat soluble vitamins deficiency and another group of neurologic signs due to vit E deficiency such as ataxia [5].

1. It is a rare disease passed down through families. The patient is unable to fully absorb dietary fats through the intestines. This is caused by a defect in a gene that tells the body to create lipoproteins (molecules of fat combined with protein). The defect makes it hard for the body to properly digest fat and essential vitamins.

2. Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS).

This patient demonstrated neuroacantocytosis characteristic presented before adulthood with orofacial dyskinesia including difficulty during eating.

Weight loss due to poor nutritional status, orofacial dyskinesia and biting lip and severe lingual damage is a major concern in these patients but in this report the weight was acceptable for his age.

Abscence seizure is usually seen in 40% of these patients but our patient had one episode of febrile convulsion in toddler period [7].

In chorea-acanthocytosis (ChAc) and McLeod Syndrome (MLS), acanthocytes are regularly seen, whereas in Huntington's disease-like2 (HDL2) and pantothenate kinase-associated neurodegeneration (PKAN), they are only occasionally observed [8].

Also, acantocytosis is found in some congenital or acquired disorders such as liver or renal insufficiency, hypothyroidism, cancers and congenital red blood cell membranopathies, [5] therefore causes of acquired acantocytosis should be rule out before bringing up of hereditary acantocytocytosis diagnosis.

Movement disorders are seen rarely in pediatric age group but may consider important disorders such as Wilson disease, extrapyramidal cerebral palsy, and rare neurodegenerative disorders or PANDA2. This point may be highlighting the significance of peripheral blood smear assessment in all cases of severe tic and dyskinetic disorders, Although), acantocytes are only occasionally observed in NAs [9].

Therefore, review of prepheral blood smear in pediatric patients with movement disorders supports diagnosis of NA syndromes.

In this patient mild splenomegaly was detected in sonography evaluations. Panthothenate kinase with neurodegenerative disease (PKAN) is an autosomal recessive disorder in the differential diagnosis of this patient with relative specific brain MRI feature (eye of tiger) [10]. MRI in our patient hadn't specific pattern. Dystonia and cognitive and behavioral changes leading clinical manifestation.

Huntington's disease is the most important differential diagnosis in patients with chorea, behavior and cognitive deficits [11]. Genetic studies for diagnosis of Huntington's disease should be necessary in all of movement disorders. This disorder may be presented with neurologic or hematologic or combined manifestations. In absence of each symptoms or in presence of one group of symptoms, the assessment for other symptoms should be done.

Conclusion

Pediatric movement disorders neuroacantosis include wide spectrum of heterogeneous disorders. These movement abnormalities and acantocytosis should be evaluate for prepheral blood smear at onset of movement disorders or periodicaly for causes of acantocytosis such as acquired liver and renal disorders, abetalipoproteinemia and Mc Leod syndrome and also other causes of movement disorder without acantocytosis include Wilson disease, Huntington disease, panthotenic acid kinase deficiency, or autoimmune neurologic disorders

Conflict of Interest: The authors declare that there is no conflict of interest.

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