Neuroacanthocytosis

Neuroacanthocytosis encompasses a group of genetically heterogenous disorders characterized by neurologic signs and symptoms associated with acanthocytosis, an abnormality of red blood cells.

The 'core' neuroacanthocytosis syndromes, in which acanthocytes are a typical feature, are chorea acanthocytosis and McLeod syndrome. Acanthocytes are seen less frequently in other conditions including Huntington's disease-like syndrome 2 (HDL2) and pantothenate kinase-associated neurodegeneration (PKAN).

The neuroacanthocytosis syndromes are caused by a range of genetic mutations and produce a variety of clinical features but primarily produce neurodegeneration of the brain, specifically the basal ganglia.

Differential diagnosis

Chorea is a hyperkinetic movement disorder characterised by excessive spontaneous movements that are irregularly timed, randomly distributed and abrupt. In this article, the authors discuss the causes of chorea, particularly Huntington's disease and the genetic syndromes that may resemble it, including HDL1-3, inherited prion disease, spinocerebellar ataxias 1, 3 and 17, neuroacanthocytosis, dentatorubro-pallidoluysian atrophy (DRPLA), brain iron accumulation disorders, Wilson's disease, benign hereditary chorea, Friedreich's ataxia and mitochondrial disease. Acquired causes of chorea include vascular disease, post-infective autoimmune central nervous system disorders (PANDAS), drugs, systemic lupus erythematosus, antiphospholipid syndrome, thyrotoxicosis, AIDS, chorea gravidarum, and polycythaemia rubra vera [1)].

Treatment

Results from the few reports of chorea-acanthocytosis patients treated with deep brain stimulation (DBS) have been inconsistent.

Li et al. present case reports for two patients with chorea-acanthocytosis who received DBS treatment and compare the outcomes with results from the literature. Both patients showed the typical clinical features of chorea-acanthocytosis with motor symptoms resistant to medical treatment. Chorea was significantly improved following low-frequency DBS treatment in both patients. However, dystonia was only mildly improved. Four chorea-acanthocytosis patients treated with DBS treatment have been reported in the literature. One patient had improvement with low-frequency DBS stimulation, while another two had improvement with higher-frequency DBS. One patient, however, did not improve with either low-frequency or high-frequency DBS. Bilateral DBS to the GPi can improve chorea and dystonia in some patients with intractable chorea-acanthocytosis. However, selection criteria for the most promising candidates must be defined, and the long-term benefits evaluated in clinical studies [2)].

see Globus Pallidus Internal Deep-Brain Stimulation in a Patient with Neuroacanthocytosis with Drug-Induced Parkinsonism [3)].

Case series

The medical files of 19 previously reported cases of neuroacanthocytosis were reviewed. Ten of the patients involved had undergone comprehensive cognitive assessments, and their neuropsychological records formed the basis of the present study.

Data on discrepancies between estimated optimal and obtained measures of general intelligence and scores on focal cognitive tests of memory, language, visual perception, and frontal lobe executive skills were tabulated and interpreted.

Eight of the patients had evidence of general intellectual deterioration. Five patients presented with memory impairment, two of whom showed visuoperceptual deficits. None of the patients showed any significant high-level language deficits. The most consistent findings across cases was evidence of impairment in frontal lobe executive skills and psychiatric morbidity.

The cognitive and psychiatric features of the patients suggests that neuroacanthocytosis is a frontosubcortical type of dementia [4)].

Case reports

A 70-year-old male patient of Greek origin with choreatic movements of the tongue and face, lower limb muscle weakness, peripheral neuropathy, elevated creatinephosphokinase (CPK), acanthocytosis and haemolysis in the absence of Kell RBC antigens with an additional Factor IX-deficiency. Genetic testing for mutations in the three exons of the XK gene revealed a previously unreported hemizygous single base-pair frameshift deletion at exon 1 (c.229delC, p.Leu80fs). In conclusion, we hereby describe a rare phenotype of a patient with McLeod syndrome which was discovered coincidentally during routine blood group testing and consecutively genetically confirmed [5)].

A 32-year-old patient with chorea acanthocytosis with a failed attempt at awake deep brain stimulation (DBS) surgery due to intraoperative seizures and postoperative intracranial hematoma. He then underwent a second DBS operation, but under general anesthesia and with intraoperative magnetic resonance imaging guidance. Marked improvement in his dystonia, chorea, and overall quality of life was noted 2 and 8 months postoperatively.

DBS surgery of the bilateral globus pallidus pars interna may be useful in controlling the hyperkinetic movements in neuroacanthocytosis. Because of the high propensity for seizures in this disorder, DBS performed under general anesthesia, with intraoperative magnetic resonance imaging guidance, may allow successful implantation while maintaining accurate target localization [6)].

Deep brain pallidal stimulation for movement disorders in neuroacanthocytosis [7)].

Patients Choreoacanthocytosis was identified in 2 Mexican mestizo sisters with healthy

consanguineous parents. Clinical manifestations began at different ages.

The onset of signs and symptoms of CHAC in the proband was at age 32 years and was characterized by balancing problems followed by chorea, compulsive lip and tongue biting with buccolingual self-mutilation, dysarthria, dysphagia, and weight loss. The first clinical manifestations in the proband's sister occurred at age 45 years and included multiple motor and verbal tics, with coprolalia, followed by lip and tongue biting, self-mutilation, and chorea. The clinical findings in both sisters were remarkable for acanthocytosis that developed late, when neurologic changes were already evident. Mutation screening of the VPS13A gene revealed homozygosity for the frameshift mutation c.3556_3557dupAC in exon 33. Currently, the proband's sister, in whom neurologic defects developed 13 years after onset of CHAC in the proband, is the least affected.

The same mutation of the VPS13A gene can be expressed differently in the same family. This observation confirms the notion that there is considerable heterogeneity in the clinical manifestation of CHAC [8].

In this 37-year-old patient clinical, biochemical and histologic data revealed a non specific primary myopathy. Other important findings were decreased levels of 5-hydroxy-indoleacetic acid (5-HILA) and homovanillic acid (HVA) in the CSF, cerebellar and basal ganglia atrophy seen in MRI and infertility of probable gonadal origin [9].

1)
Wild EJ, Tabrizi SJ. The differential diagnosis of chorea. Pract Neurol. 2007 Nov;7(6):360-73. Review. PubMed PMID: 18024776.
2)
Li P, Huang R, Song W, Ji J, Burgunder JM, Wang X, Zhong Q, Kaelin-Lang A, Wang W, Shang HF. Deep brain stimulation of the globus pallidus internal improves symptoms of chorea-acanthocytosis. Neurol Sci. 2012 Apr;33(2):269-74. doi: 10.1007/s10072-011-0741-y. Epub 2011 Aug 24. PubMed PMID: 21863267.
3)
Doshi P, Chamankar N. Globus Pallidus Internal Deep-Brain Stimulation in a Patient with Neuroacanthocytosis with Drug-Induced Parkinsonism. Stereotact Funct Neurosurg. 2018 Aug 28:1. doi: 10.1159/000492234. [Epub ahead of print] PubMed PMID: 30153676.
4)
Kartsounis LD, Hardie RJ. The pattern of cognitive impairments in neuroacanthocytosis. A frontosubcortical dementia. Arch Neurol. 1996 Jan;53(1):77-80. PubMed PMID: 8599563.
5)
Wiethoff S, Xiromerisiou G, Bettencourt C, Kioumi A, Tsiptsios I, Tychalas A, Evaggelia M, George K, Makris V, Hardy J, Houlden H. Novel single base-pair deletion in exon 1 of XK gene leading to McLeod syndrome with chorea, muscle wasting, peripheral neuropathy, acanthocytosis and haemolysis. J Neurol Sci. 2014 Apr 15;339(1-2):220-2. doi: 10.1016/j.jns.2014.01.034. Epub 2014 Feb 1. PubMed PMID: 24529944; PubMed Central PMCID: PMC3988988.
6)
Lim TT, Fernandez HH, Cooper S, Wilson KM, Machado AG. Successful deep brain stimulation surgery with intraoperative magnetic resonance imaging on a difficult neuroacanthocytosis case: case report. Neurosurgery. 2013 Jul;73(1):E184-7; discussion E188. doi: 10.1227/01.neu.0000429852.45073.73. PubMed PMID: 23615095.
7)
Guehl D, Cuny E, Tison F, Benazzouz A, Bardinet E, Sibon Y, Ghorayeb I, Yelnick J, Rougier A, Bioulac B, Burbaud P. Deep brain pallidal stimulation for movement disorders in neuroacanthocytosis. Neurology. 2007 Jan 9;68(2):160-1. PubMed PMID: 17210902.

8)
Ruiz-Sandoval JL, García-Navarro V, Chiquete E, Dobson-Stone C, Monaco AP, Alvarez-Palazuelos LE, Padilla-Martínez JJ, Barrera-Chairez E, Rodríguez-Figueroa EI, Pérez-García G. Choreoacanthocytosis in a Mexican family. Arch Neurol. 2007 Nov;64(11):1661-4. PubMed PMID: 17998451.
9)
Gil-Nagel A, Morlán L, Balseiro J, García de Yébenes J, Cabello A, Martínez-Martín P. [Neuro-acanthocytosis with associated myopathy. A case report]. Neurologia. 1994 Apr;9(4):165-8. Spanish. PubMed PMID: 7517146.