



Diagnostic Challenges of Auto Mutilations: A Case Report

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Abstract

Auto-mutilation is a common psychiatric behavior disorder. However, it could be the revealing sign of a rare neurological disease such as neuroacanthocytosis. Therefore, we will discuss the neurological origin of auto-mutilations through the illustration of a clinical case of a 39-year-old woman who consulted the psychiatry department of Sousse in 2016 for behavioural disorders. She had not previous history of neurological disease. She developed insidious oral auto-mutilations. She was examined by dermatologists and psychiatrists, but no etiology was retained.

A few months later, she developed movement disorders and the neurological examination has concluded to choreic movements interesting the head and upper limbs, tendon areflexia and cognitive impairment. Blood smear revealed acanthocytes (9%). Biological assessment showed a high level of muscular enzymes (CPK=1000IU/L, LDH=600IU/L). Cerebral MRI showed an atrophy of caudal nuclei. The EMG concluded to a sensitive-motor axonal neuropathy, predominant in inferior limbs. The diagnosis of neuroacanthocytosis was retained and the treatment was mainly symptomatic (Neuroleptics and vitamins).

Neuroacanthocytosis is a rare affection with a polymorphous clinical expression. We should consider that affection even with isolated inaugural psychiatric signs.

Keywords

Auto-mutilation; Neuroacanthocytosis; Diagnostic; Challenges

Introduction

Neuroacanthocytosis (NA) syndromes are a group of genetically defined diseases characterized by the association of red blood cell acanthocytosis and progressive degeneration of the basal ganglia. NA syndromes are exceptionally rare with an estimated prevalence of less than 1 to 5 per 1'000'000 inhabitants for each disorder [1].

Neuroacanthocytosis (NA) refers to a heterogeneous group of syndromes in which nervous system abnormalities coincide with red blood cell acanthocytosis, i.e. deformed erythrocytes with spike-like protrusions [2]

The core NA syndromes include autosomal recessive chorea-acanthocytosis (ChAc) and X-linked McLeod syndrome which have a Huntington's disease-like phenotype consisting of a choreatic movement disorder, psychiatric manifestations and cognitive decline, and additional multi-system features including myopathy and axonal neuropathy. In addition, cardiomyopathy may occur in McLeod syndrome.

ChAc is a progressive autosomal recessive neurodegenerative disorder with onset of neurological symptoms usually in the twenties, thus representing a late onset for an autosomal recessive disorder [2]. Often the initial presentation may be subtle cognitive or psychiatric symptoms, and in retrospect patients may have developed related psychiatric complaints several years before the neurological manifestations. Impairment of memory and executive functions is frequent, although not invariable. Psychiatric manifestations are common and may present as schizophrenia-like psychosis or obsessive-compulsive disorder.

Faced with this heterogeneity of symptoms and these varieties, making the right diagnosis would be a challenge.

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Case report

We report the case of a female patient aged of a 39 year-old, without previous history of neurological disease. She is born to Consanguineous Parents (Figure 1).



Figure 1: She developed insidious oral auto-mutilations

She was examined and followed by dermatologists and psychiatrists. No etiology was retained. She developed few months' later movement disorders. Neurological examination has concluded to choreic movements interesting the head and upper limbs, tendon areflexia and cognitive impairment.

Biological assessment showed a high level of muscular enzymes (CPK=1000IU/L, LDH=600IU/L) (Figure 2,3).

The EMG concluded to a sensitive-motor axonal neuropathy, predominant in inferior limbs. Genetic assessment for Huntington disease was negative. We retained the diagnosis of neuroacanthocytosis and the treatment was mainly symptomatic (Neuroleptics and vitamins)

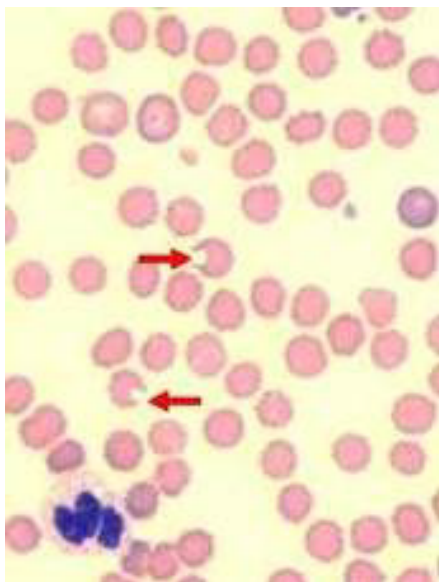


Figure 2: Blood smear revealed 09% of acanthocytes

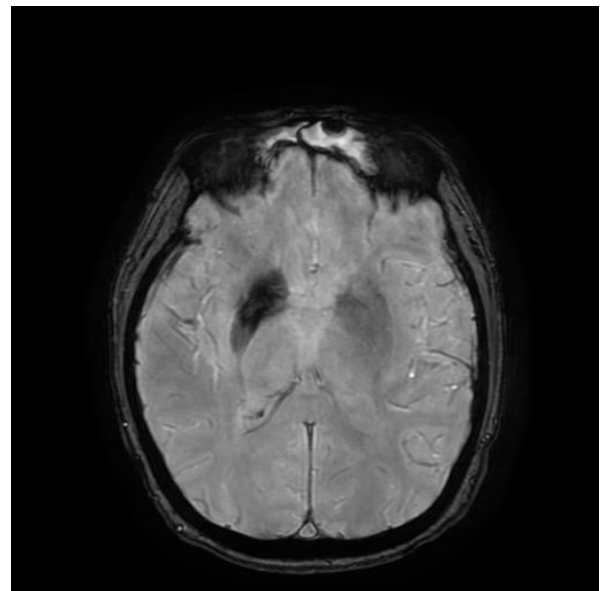


Figure 3: Cerebral MRI showed an atrophy of caudal nuclei

Results

Neuroacanthocytosis is an autosomal recessive affection, with a progressive evolution. It appears often in young male adults and rarely among women such in our case. Clinical symptoms include movement disorders (chorea, oro-facial dyskinesia and oro-lingual auto-mutilations), peripheral neuropathy and frontal dementia.

During the disease course, our patient was developed a characteristic phenotype including chorea, a very peculiar "feeding dystonia" with tongue protrusion, orofacial dyskinesias, involuntary vocalizations, dysarthria and involuntary tongue- and lip-biting. This has been cited in the literature [5].

The gait of ChAc patients may have a "rubber man" appearance with truncal instability and sudden, violent trunk spasms [6]. In addition to orofaciolingual dystonia, limb dystonia is common. In at least one third of patients, seizures, typically generalized, are the first manifestation of disease[5]

Most ChAc patients have elevated levels of creatine phosphokinase (CK). In contrast to MLS (McLeod Neuroacanthocytosis Syndrome), myopathy and axonal neuropathy are usually mild.

Clinical neuromuscular manifestations include areflexia, sensory-motor neuropathy, and variable weakness and atrophy. Muscle biopsy and electromyography commonly demonstrate neuropathic changes and rarely myopathic alterations.

Aetiology

The genes responsible for the various NA syndromes have been identified. ChAc is caused by various mutations of a 73 exon gene on chromosome 9, VPS13A, coding for chorein [3,4]. No obvious genotype-phenotype correlations have been observed. Chorein is implicated in intracellular protein sorting but its physiological functions are not yet known. Chorein is widely expressed throughout the brain and various internal organs. Almost all mutations to date appear to result in absence of chorein and there do not appear to be any partial manifestations of the disease, e.g. in heterozygous carriers.

On the other hand, Huntington's disease like 2 (HDL 2) is caused by expanded trinucleotide repeats of the junctophilin 3 gene (JPH3). As in Huntington's disease (HD), there is anticipation and the age of onset is inversely related to the size of the trinucleotide repeat expansion. Affected individuals have CTG/CAG repeat expansions of 41-59 triplets (normal population: 6-27). The expanded trinucleotide repeat in the JPH3 gene responsible for HDL2 causes both

ubiquitinated intranuclear neuronal inclusions [7-9] and cytoplasmic mRNA inclusions [10]. There is evidence from cell culture studies that these latter inclusions are responsible for cell death [10].

Diagnostic considerations

Research of acanthocytes in blood smear is important for diagnosis showing a percentage above 5%. Sometimes, the determination of acanthocytosis in peripheral blood smears may be negative in a standard setting and a negative screen does not exclude an NA syndrome [11]. Automated blood counts usually show an elevated number of hyperchromic erythrocytes. A more sensitive and specific method for the detection of acanthocytes uses a dilution with physiological saline and phase contrast microscopy [12]. In contrast to the often elusive acanthocyte search, serum CK is elevated in most cases of ChAc and MLS and the persistent elevation of CPK is usual.

HDL2 and HD have similar symptoms but with certain differences. HDL2 presents usually in young adulthood, but, as with HD, the age of onset is inversely related to the size of the trinucleotide repeat expansion [10]. Patients may develop psychiatric abnormalities as the initial manifestation, with later appearance of chorea, Parkinsonism and dystonia [13]. The disease may evolve from chorea to a more Bradykinetic, dystonic phenotype, or remain parkinsonian throughout the disease course, but unlike HD, this is not related to the size of the trinucleotide expansion. Unlike in ChAc and MLS, deep tendon reflexes are usually brisk; there are no peripheral nerve or muscle abnormalities, and seizures have not been reported. Acanthocytosis is found in about 10% of HDL2 patients and CK levels are normal. 8/9 Neuroimaging reveals bilateral striatal atrophy, in particular of the caudate nucleus. In contrast to ChAc and MLS, generalized cortical atrophy may develop during the disease course. Neuropathologically, ubiquitin-immunoreactive intranuclear neuronal inclusions, similar to those seen in HD, are found [10].

In ChAc and MLS, electroneurography may demonstrate sensorimotor axonal neuropathy whereas electromyography may show neurogenic as well as myopathic alterations. Neuroradiologically, there is progressive striatal atrophy especially affecting the head of caudate nucleus and impaired striatal glucose metabolism similar to that seen in HD (Figure 3) [14,15] (Figure 4 A-H).

Treatment

So far no curative or disease-modifying treatments are available and management of the NA disorders is purely symptomatic. Treatment is mainly based on vitamins, neuroleptics and psychotherapy.

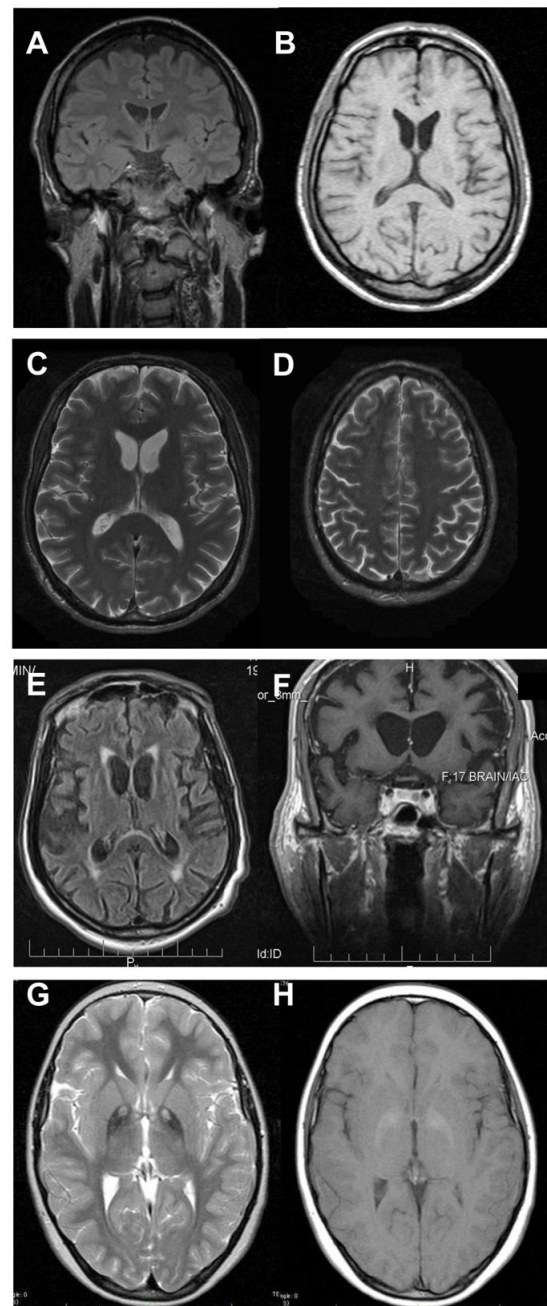
Recognition of treatable complications such as seizures, swallowing problems, and heart involvement is essential. Neuropsychiatric issues, particularly depression, can have a major impact upon quality of life, and these symptoms may be more amenable to pharmacotherapy than others. Dopamine antagonists or depleters 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. Low frequency stimulation (40Hz) improved chorea, but not dystonia.

Non-medical therapies with a multidisciplinary approach are often helpful. Evaluation by a speech therapist is essential to minimize problems due to dysphagia and weight loss. Dystonia of the lower face and tongue can result in severe tongue and lip self-mutilation in ChAc and may be ameliorated by a bite plate. Most importantly, extended and continuous multidisciplinary psychosocial support should be provided for the patients and their families.

Administration of neuroleptics for psychiatric disease may confound the recognition of the appearance of movement disorders by as much as a decade [5].

Prognosis and evolution

ChAc usually slowly progresses over 15-30 years, but sudden death, presumably caused by seizures or autonomic involvement,



Neuroimaging: *ChAc*. Coronal FLAIR- (A) and axial T1-weighted (B) images demonstrate moderate atrophy of the caudate nucleus. *MLS*. Axial T2-weighted images demonstrate moderate atrophy of caudate nucleus and putamen (C) but no relevant cortical atrophy (D). *HDL2*. Axial FLAIR- (E) and coronal T1-weighted images (F) demonstrate atrophy of the caudate nucleus and the fronto-temporal cortex. In addition, FLAIR images show periventricular white matter hyper-intensities (courtesy of Nora Chan, MD, UCLA, and Los Angeles, USA). *PKAN*. T2-weighted fast spin echo (G) and T1-weighted (H) brain MRI scans from a child with PKAN demonstrating the “eye of the tiger” sign (courtesy of Susan J. Hayflick, MD, Oregon Health and Science University, Portland, Oregon, USA).

may occur. All NA disorders have a relentlessly progressive course and are eventually fatal. Sudden death may be due to seizure, or possibly autonomic dysfunction, but there may be gradually progressive, generalized debility, as seen in Huntington's or Parkinson's diseases, with patients succumbing to aspiration pneumonia or other systemic infections.

Conclusion

Neuroacanthocytosis a rare affection with a polymorphous clinical expression. We should consider that affection even with isolated inaugural psychiatric signs.

NA syndromes must be included in the differential diagnosis of Huntington disease (HD). Their consideration is mandatory if HD genetic testing is negative. The NA syndromes have additional clinical characteristics such as epilepsy, peripheral neuropathy, cardiomyopathy (MLS) as well as orofacial dyskinesia, and feeding dystonia (ChAc). Paraclinical findings such acanthocytosis and elevated CK levels may be crucial to indicate the appropriate laboratory examination, in particular Kell blood group phenotyping and chorein Western blotting. Specific genetic testing may confirm the diagnosis. Management of NA syndromes is symptomatic, although life expectancy and quality of life may be augmented considerably by the appropriate measures.

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