Seizures of extratemporal origin as a prominent feature in a Tamilian male with chorea-acanthocytosis

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PURPOSE: Temporal lobe epilepsy as a presenting feature of choreoacanthocytosis (ChAc) was described recently (Al-Asami et al., Epilepsia, 2005; 46: 1256 – 1263) We report on a Tamilian male suffering from ChAc with seizures in order to add information concerning the epileptological phenotype of ChAc. Furthermore, his family history raises the question of possibly autosomal dominant transmission of this usually autosomal recessive condition.

CASE REPORT: m, *1969

Family history: see pedigree (Fig. 1)

Signs and Symptoms

- Normal birth and developmental milestones, higher school education
- Paranoide psychosis since the age of 34 y, cured by neuroleptic medications
- Epilepsy since the age of 34 y
  - Secondary generalised seiuzres (?)
  - Complex partial seizures during night: initial feeling of confusion, then loss of consciousness, hypermotory or tonic signs, vocalization
  - With adequate drug treatment probably seizure free, seizure recurrence due to non-compliance
  - PHT and OXC seem to be effective
- Involuntary thoung movements, later short involuntary vocalisations and movements of the feet, oro-facial dyskinesias, eye blinking since the age of 35 y
- Cognitive decline, change of personality
- Other neurological signs: weak tendon reflexes on upper extremities, lost tendon reflexes on lower extremities
- Despite a clear wish for having children the couple had only probably two miscarriages of unknown gender so far

Paraclinical Findings

- Neuropsychology:
  - 03/05: mild impairment of episodic verbal- and non-verbal memory, very mild impairment of attention and executive functions
  - 06/06: progressive impairment of speech dominant hemisphere
- EEG: (Fig. 2)
  - Inerictal: sharp waves left posterior temporal, bioccipital; 7Hz background activity
  - Ictal: no seizure pattern detectable, muscle artifacts during hypermotor siezures
- Neurography: N. suralis (r/l): CV reduced, N. tibialis (r), N. peroneus (r): normal, N. tibialis (l): dml at limit
- EMG: M. vastus lat (r) normal, M. biceps brachii (r) normal
- ECG:
  - 1-channel ECG in EEG: intermittent VES, bradycardia, asystolia lasting 5 s
  - 24-h-ECG: 38-140/min, VES as short bigemini, supraventricular ES
- Echocardiography: normal
- MRI: between 03/05 and 06/06 non-progressive atrophy of nucleus caudatus beside mild supratentorial and infratentorial brain atrophy (Fig.3)
- FDG-PET 6/05: Bilateral nigrostriatal Hypometabolism
- Laboratory tests:
  - Pathological routine tests: CK 942 U/l, GPT 59 U/l, GOT 82 U/l, GGT 55 U/l, Cholesterin 6.2 mmol/l
  - Pathological in special tests: TSH 4.64 mU/l (elevated) (3/05) and 2.94 mU/l (normal) (6/06), Anti-TPO 149 – 298 IE/ml (< 100); low testoteron, low SHBG; ANA 1:160 (3/05), 1:320 (6/06) (< 1:80)
  - Normal in special tests: Thyreoglobulin antibodies, and otherautoantibodies
- Molecular Genetics excluded mutations in
  - HD
  - HDL1 (=PrP)
  - HDL2 (=Junctophylline 3)
  - DRPLA
  - SCA 3
- Hematology:
  - Normal findings in Kell antigene analysis, no acanthocytes in blood (standard test, no dilution)
  - Acanthocytes in a wet preparation of diluted blood (Tab)
  - Impaired chorein expression in red blood cells (Fig. 4)

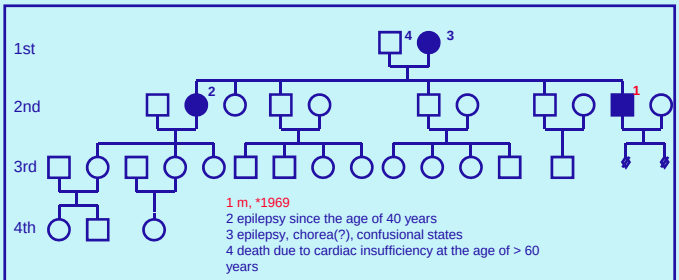

Fig. 1: Pedigree obtained in 11/06. Mind that the oldest person in the 3rd generation is 32 y

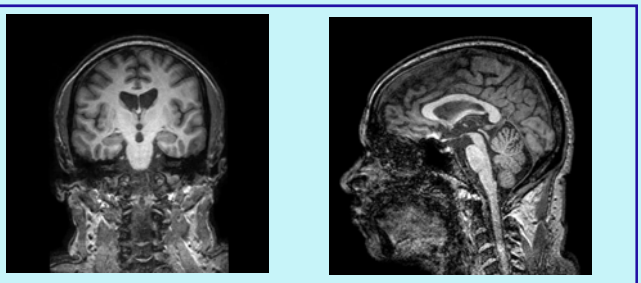

Fig. 3: MRI showing distinct atrophy of nucleus caudatus, mild supratentorial atrophy and normal hippocampi in the coronar section and mild cerebellar atrophy in the sagittal section

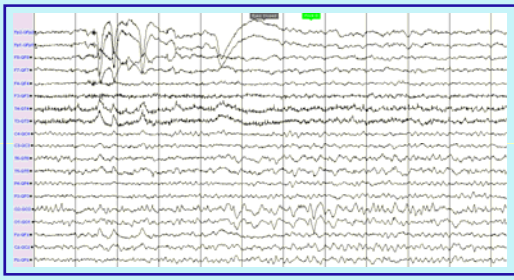

Fig. 2: EEG showing occipital sharp waves and slow background activity

Time (min)	EDTA		Heparin	
	Patient	Control	Patient	Control
0	4.5	0	7.4	0
30	6.7	0.6	8.3	0.9
120	8.5	1.25	12.2	2.3

Tab. : Percentage of acanthocytes in a diluted wet preparation of blood from the patient and from a control

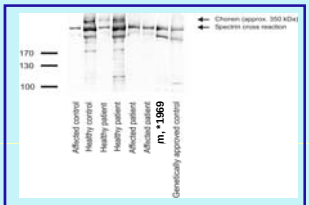

Fig. 4: Western blot of chorein expression

DISCUSSION:

- Chorea, psychosis, cognitive decline and epilepsy together with the family history point to a hereditary neurodegenerative disease
- After HD, HDL1, HDL2, DRPLA and SCA3 have been ruled out by molecular genetic tests ChAC was considered
- Whereas standard blood tests failed to demonstrate acanthocytes these were disclosed in wet preparations of diluted blood
- Finally, western blot revealed markedly impaired chorein expression proving ChAC
- Molecular genetic studies of the VPS13A gene are ongoing in order to define genotype and mode of inheritance which seems to be autosomal dominant in our case

CONCLUSION:

- ChAC can also be found in the Tamilian population
- Beside temporal lobe epilepsy extratemporal seizures can also belong to the epiletological phenotype of ChAc
- Epileptologists should consider ChAc as possible etiology in (hereditary) epilepsies especially if there are chorea and psychiatric symptoms beside seizures
- There may be autosomal dominant inheritance in ChAc