Neurologist-in-training

The aim of this section is to prepare the neurologist-in-training for the FMH examination, to confront her or him with specific problems of everyday neurological practice and to give him or her updates on recent controversies in clinical neurology.

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Case vignette

The 60-year-old right-handed man, originating from Serbia, was sent for a neurological consultation because of a gait disorder. His son and his ex-wife reported changes of his personality, difficulties to articulate and a peculiar gait since several years. Because of a depression he was in ambulatory psychiatric care. He had lost 30 kilogrammes of body weight in the last 3 years and reported to have troubles to fall asleep. At the time of the first consultation, he had a medication with diazepam 10 mg per day. Due to his health problems, his relatives doubted that he could live alone in his apartment in the future. At admission he was fully oriented, he had an impaired short-term memory and was in a depressive mood. Neurological examination revealed no oculomotor abnormalities, no sensory-motor deficits and a normal coordination. Tendon reflexes were brisk, plantar responses were flexor. Gait was broad based without clear gait ataxia. There was a generalised hyperkinesia of limbs and to a lesser extent of the face and the trunk with sudden brisk movements considered as choreatic movements.

Question 1

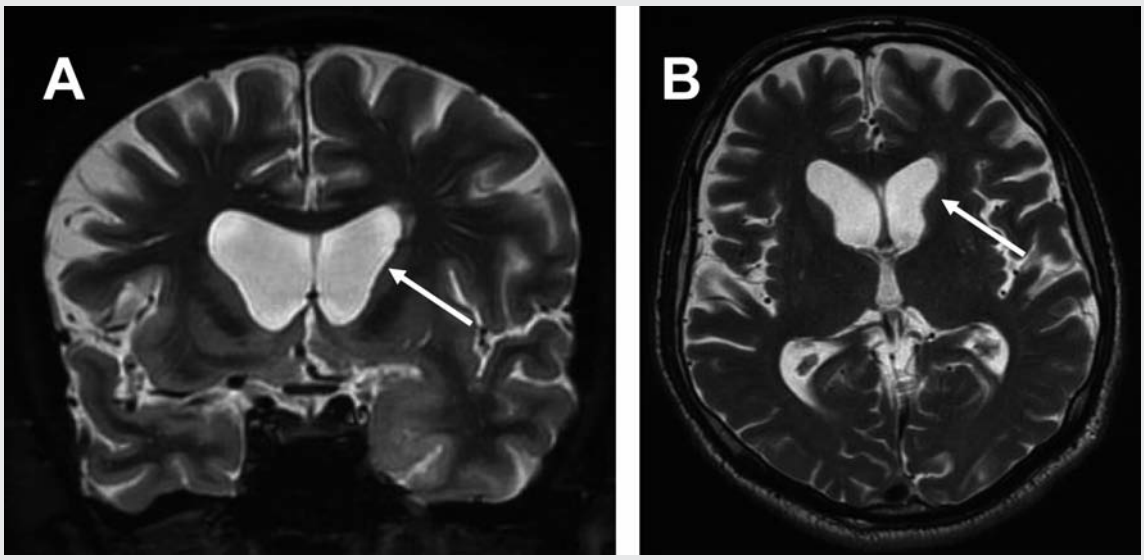
What are possible causes of a choreatic movement disorder?

Question 2

Which are the components of a chorea syndrome?

Question 3

What are symptomatic treatments of chorea?



Additional examinations

Due to the history of the patient, a paraneoplastic chorea syndrome was suggested. Extensive work-up including chest- and abdomen-computed tomography as well as determination of anti-neuronal paraneoplastic antibodies was negative. Blood smears did not reveal erythrocyte acanthocytosis. Immunological evaluation including anti-double-stranded DNA antibodies and anti-phospholipid antibodies was negative. Cerebral magnetic resonance imaging revealed a slight atrophy of the head of the caudate nucleus with consecutive enlargement of the lateral ventricles which is obvious in the coronal sections but not necessarily in the axial sections (arrows, fig. 1A and 1B). FDG-positron emission tomography showed a severely impaired striatal FDG uptake. Because of the negative evaluation of a symptomatic chorea syndrome, a neurodegenerative chorea syndrome was suspected. After appropriate genetic counselling a molecular genetic analysis of the huntingtin gene was performed, demonstrating 43 CAG repeats in the huntingtin gene.

Table 1. Neurodegenerative chorea syndromes.

disorder	inheritance	chromosome	gene	phenotype
Huntington's disease	AD	4p16.3	huntingtin	chorea syndrome
HDL1	AD	20pter-p12	prion-protein	chorea syndrome
HDL2	AD	16q24.3	junctophilin-3	chorea syndrome
HDL3	AR	4p15.3	unknown	chorea syndrome
HDL4	AR	6q27	TATA box-binding protein	chorea syndrome
SCA 17				ataxia
				parkinsonism
				dystonia
SCA1	AD	6p23	ataxin-1	chorea syndrome
				ataxia
				slow saccades
				polyneuropathy
DRPLA	AD	12p13.31	atrophin-1	chorea syndrome
				ataxia
				myoclonus epilepsy
choreo-acanthocytosis (ChAc)	AR	9q21	chorein	chorea syndrome
				erythrocyte acanthocytosis
				dystonia
				parkinsonism
				myopathy
				axonal neuropathy
McLeod's syndrome	X-linked	Xp21.2-p21.1	XK protein	chorea syndrome
				erythrocyte acanthocytosis
				epilepsy
				myopathy
				cardiomyopathy
				axonal neuropathy
benign hereditary chorea (BHC)	AD	14q13	thyroid transcription factor-1	isolated childhood-onset chorea

(For correct answers, see page 80)

Diagnosis

Huntington's disease.

Epicrisis

Treatment with tiapride (Tiapridal®) 3 × 100 mg and mirtazepine (Remeron®) 1 × 30 mg was initiated. After 3 months sleep quality had considerably improved, the choreatic movement disorder was less pronounced, and he could still live in his own apartment with minor support of relatives and the local social service.

Take-home message

- → **A choreatic movement disorder may have different aetiologies including several treatable entities.**
- → **A hereditary neurodegenerative chorea syndrome may be present in the absence of an obvious family history.**
- → **Although hereditary neurodegenerative chorea syndromes are relentlessly progressive fatal disorders, a symptomatic treatment may be beneficial and can improve the quality of life of patients and relatives.**

Suggested reading

Cardoso F, Seppi K, Mair KJ, Wenning GK, Poewe W. Seminar on choreas. Lancet Neurol. 2006;5:589–602.

Jung HH. Differentialdiagnose hereditärer Chorea-Syndrome. Schweiz Arch Neurol Psychiatr. 2002;153:185–8.

Walker FO. Huntington's disease. Lancet. 2007;369:218–28.

Walker RH, Jung HH, Dobson-Stone C, Rampoldi L, Sano A, Tison F, et al. Neurologic phenotypes associated with acanthocytosis. Neurology. 2007;68:92–8.

Answer 1

Choreatic movements may be the consequence of an inflammatory alteration of the basal ganglia in the context of a rheumatic fever, a systemic lupus erythematodes or a phospholipid antibody syndrome. Rarely, choreatic movement disorders have been described as a paraneoplastic syndrome. A choreatic movement disorder may arise as a side effect of medications such as neuroleptics. Structural brain lesions of the striatum or the subthalamic nucleus such as an ischaemia haemorrhage or a brain tumour may cause haemichorea or hemiballism. Tic disorders or psychogenic movement disorders may have chorea-like features. Finally, a choreatic movement disorder may be a symptom of a neurodegenerative chorea syndrome (table 1).

Answer 2

Choreatic movement disorder
Chorea is the ancient Greek word for "dancing". A choreatic movement disorder is defined as rapid, irregular, spontaneous movements which arise accidently and abruptly flow from one part of the body to the other. Choreatic movement may be incorporated in voluntary movements such as in the milkman grip sign.

Psychiatric manifestations
Psychiatric manifestations are frequent in chorea syndromes and may precede motor or cognitive manifestations. Psychiatric manifestations may include changes of personality, affective disorders, obsessive-compulsive disorders as well as manic and psychotic symptoms.

Cognitive decline
Cognitive dysfunction in chorea syndromes often spares long-term memory but impairs executive functions, such as organising, planning, checking or adapting alternatives, and delays the acquisition of new motor skills. Anosognosia is often evident.

Answer 3

Choreatic movement disorders may be ameliorated by dopamine antagonists or dopamine deleting drugs. First-line medications are dopamine antagonistic neuroleptics such as tiapride (Tiapridal®), 3 × 100 mg to 3 × 400 mg per day, or sulpiride (Dogmatil®), 2 × 50 mg to 2 × 400 mg per day. Other neuroleptic drugs with antichoreatic effect are clozapine (Leponex®), 3 × 6.25 to 3 × 25 mg, or haloperidole (Haldol®), 3 × 0.5 to 3 × 2 mg. Because of the high risk of tardive dyskinesias or other extrapyramidal side effects, however, haloperidole is reserved for severe, otherwise untreatable choreatic movement disorders. An alternative to the neuroleptic drugs is the dopamine depleting drug tetrabenazine (Nitoman®), 25 to 100 mg per day. A relevant possible adverse effect is the development of a depression. Tetrabenazine is not approved in Switzerland, but there is an approval for the treatment of choreatic movement disorders in Germany. It may be prescribed as an "orphan drug" for the treatment of a choreatic movement disorder after approval of assumption of costs by the health insurance.