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Short Communication

Liquorpheresis (CSF filtration) in familial amyotrophic lateral sclerosis

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Objectives: Liquorpheresis (CSF filtration) has been shown to be of benefit in various neurologic disorders, including sporadic ALS. Liquorpheresis in patients with familial ALS, has not been investigated so far.
Methods: A 52-year-old woman with familial ALS is reported who underwent liquorpheresis during 4 consecutive days. During this period, 875 ml CSF were filtered off via an intrathecal catheter and a combined mechanical and ionic filter by means of a bi-directional syringe pump.
Results: Immediately after treatment and 2 weeks later there was subjective, but no objective, improvement of her symptoms, assessed by the Norris score and measurements of the elbow extension, vital capacity, F-waves of both ulnar nerves and automatic EMG of the right brachial biceps and anterior tibial muscles.
Conclusion: Liquorpheresis does not seem to be helpful in the treatment of familial ALS.

Keywords: familial amyotrophic lateral sclerosis; liquorpheresis; peak-ratio interference pattern analysis; motor neuron disease; CSF filtration; paraparesis

Introduction

Liquorpheresis (cerebrospinal fluid (CSF) filtration) has been shown to be of benefit in various neurologic disorders, including sporadic amyotrophic lateral sclerosis (ALS).[1–3] The therapeutic effect in these disorders is said to be due to the removal of toxic metabolites, cells, inflammatory mediators or antibodies.[2,3] In familial ALS, which accounts for up to 10% of all ALS patients, liquorpheresis has not been applied so far.

Case report

We report the data of a 52-year-old woman, with a three-and-a-half-year history of slowly progressive weakness of the lower limbs. After clinical, laboratory, electrophysiological and imagery examinations, the diagnosis of probable ALS was established according to the E1 Escorial criteria.[4] Since both her mother and sister had died from ALS at the age of 51 and 48 years respectively, familial ALS was assumed. Both daughters of the patient, 28 and 32 years old, were clinically unaffected. Screening of all five SOD-1 gene exons for mutations, using a polymerase chain reaction (PCR) single-stranded conformational polymorphism (SSCP), failed to detect any abnormal patterns on two separate occasions in all three women. The negative result does not exclude familial ALS, because only 20–30% of the families have SOD-1 mutations.[5]

At presentation, the patient was able to walk unaided but with frequent pauses and occasional falls on an even floor. She could not climb stairs and after falls she was unable to get up without support. She had been on riluzole, 100 mg/day, for 1 year. On neurologic examination, the jaw jerk was hyperactive but tongue and speech were unaffected. In the upper limbs, muscle strength was normal but skilled left hand movements were disturbed. Deep tendon reflexes were hyperactive and the small hand muscles were atrophic bilaterally. No fasciculations or sensory disturbances could be observed. Concerning the lower extremities, paraparesis (MRC grade 4) and wasting with distal accentuation and absent deep tendon reflexes were found. The plantar response was extensor on the left and mute on the right side. Fasciculations could be observed in both anterior tibial muscles.

Liquorpheresis was carried out via an intrathecal 18G catheter and a bi-directional syringe pump (Flofors®, Infors AG, Bottmingen, Switzerland) and a mechanical/ionic filter (CSF-1®, Pall, Dreieich, Germany). Within 4 days, 875 ml CSF, 200–250 ml/day, were filtered off. After two filtrations, the patient reported an improvement in stabilising the knees

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during exercise. Subjectively, transfers became safer and fatigability during exercise decreased. Four days after the last filtration she fell but could get up from the floor by herself. Fourteen days after therapy she had regained the ability to climb a maximum of 20 stairs with pulling. Three weeks after the last filtration, the subjective improvement had vanished. To objectively assess the therapeutic effect of liquorpheresis, the Norris score was applied and measurements of vital capacity and elbow extension force (by means of a hand-held dynamometer), F-wave examinations of the left and right ulnar nerves and peak-ratio EMG interference pattern analysis[6] of the right brachial biceps and anterior tibial muscles were carried out before and 1, 7 and 14 days after finishing therapy. The results of these investigations showed liquorpheresis to be of little help (Table 1). Except for headache at the beginning of the first two filtrations and occasional paraesthesias in both legs, the course of the therapy was uneventful. CSF examination after the last filtration revealed only mild pleocytosis (62/3, normal: −12/3) and a discrete increase of protein (64 mg%, normal: 15–45 mg%).

Discussion

Contrary to previous reports, liquorpheresis led to a subjective but not objective improvement of motor abilities in the presented patient with familial ALS.[1,2] The reported subjective improvement was interpreted as being due to a placebo effect. Arguments for a placebo effect are the rapidity of the improvement and the fact that it lasted only for 2 weeks. All applied tests failed to confirm the subjective benefit. The slight increase of the Norris score immediately after therapy was within the intertest variability as well as the fluctuations of the force measurements, the F-wave results and those of the automatic EMG. Whether electromyography is capable of documenting a possible benefit only a few days after therapy, remains doubtful.

Table 1 Clinical and instrumental findings before and 1, 7 and 14 days after CSF filtration in a patient with familial ALS

Test	*BT*	*1 DAT*	*7 DAT*	*14 DAT*
Norris score (%)	85	89	91	87
REE (Nm)	12.7	11.3	14.3	11.8
LEE (Nm)	11.2	11.8	12.9	10.1
VC (l)	2.56	2.90	3.20	3.18
RUNP	9.5	9.5	7.5	8.0
LUNP	10	8.5	9.0	7.5
PRBB	0.74	0.76	0.80	0.72
PRTA	0.41	0.39	0.47	0.49

BT: before therapy, DAT: days after therapy, REE/LEE: maximum force at right/left elbow extension, VC: vital capacity, RUNP/LUNP: F-wave persistence of the left/right ulnar nerve, PRBB/PRTA: peak-ratio of the right brachial biceps/anterior tibial muscle, Nm: Newton meter, l: liter

No reliable data concerning this question are available so far. The improvement of the vital capacity after the first week could be attributed to a learning effect.

The different therapeutic effect of liquorpheresis in sporadic and familial ALS could be explained by the different pathogenic background of sporadic and familial ALS. In sporadic ALS, factors like AMPA/kainate, C4d, superoxide radicals, microglia antibodies, glutamate, sodium-channel blocking agents or unknown toxins are suspected to play a pathogenic role, but it is unclear if these factors are responsible for the development of familial ALS as well.[7–9] Furthermore, it is unknown if removal of these pathogenic factors by liquorpheresis is possible and if it is responsible for the reported therapeutic benefit. Only the possibility that these factors or other unknown blocking CSF components could be responsible for the development of familial ALS and the lack of any other effective therapy, justified the application of liquorpheresis in the presented patient.

Limitations of the study were that only a single patient was investigated, that the data were uncontrolled and that there was no prior hypothesis as to how big a change could be expected.

Though liquorpheresis is easily applicable and without major side effects, it does not seem to be effective in patients with familial ALS.

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