the time to reach threshold was too long and the response was not recorded. Blood work useful in clarifying the diagnosis includes creatine kinase, thyroid functions and calcium channel antibodies. Because of the high incidence of lung cancer associated with LEMS, a chest computed tomography or magnetic resonance to look for cancer needs to be part of the evaluation.

Treatment of LEMS depends on the etiology of the disease. When associated with cancer, treating the cancer will usually improve symptoms significantly. It has been demonstrated that calcium channels in the cancer cells cross-react with the presynaptic voltage-gated calcium channels. Removal of the cancer may reduce the autoimmune response and antibody production. Regardless of the presence of cancer, using immunosuppressive drugs such as azathioprine and prednisone are useful but not as helpful when compared with their use in treating other autoimmune diseases. Intravenous immunoglobulin has also been used with some success. Pyridostigmine, an anticholinesterase inhibitor, can also reduce symptoms. Inhibition of acetylcholinesterase will decrease the amount of breakdown of Ach, thus increasing the amount found in the synaptic cleft. This increase in Ach concentration allows more end-plate potentials to reach threshold, resulting in a larger number of action potentials and greater muscle contraction. Plasma exchange has been used to filter out the antibodies causing the disease and has been suggested to be the first line of treatment in acute situations. The use of plasma exchange has had limited success because the benefit dissipates more quickly than in other diseases such as MG. It has been suggested that immunosuppressive drugs are needed to maintain the benefits of plasma exchange. Another drug used for the treatment of LEMS is 3,4-diaminopyridine (3,4-DAP). 3,4-DAP is a potassium channel blocker, which helps to maintain depolarization of the nerve terminal by preventing repolarization. This allows more calcium to enter the nerve terminal and release more Ach. If cancer has not been found in patients presenting with LEMS, they should be screened for small cell lung carcinoma every 6 months with chest imaging for at least 2 years. In addition, evaluation for other autoimmune disorders should be done.

УДК 616.74-009.125-08

INTRAVENTRICULAR CERLIPONASE ALFA FOR CLN2 DISEASE

Karunakaran Naresh

Supervisor: Ph. D., Ass. Prof. ***N .N. Usava***

Establishment of Education
«Gomel State Medical University»
Gomel, Republic of Belarus

Introduction

Neuronal ceroid lipofuscinosis type 2 (CLN2) disease, a form of Batten's disease, is a rare, autosomal recessive, pediatric neurodegenerative disease resulting from pathogenic variants in the gene encoding lysosomal enzyme tri-peptidyl peptidase 1 (*TPP1*). A deficiency of TPP1 results in accumulation of lysosomal storage material that causes degenerative changes in neurons throughout the central nervous system and retina. Affected children are functionally normal until the age of 2 to 4 years and subsequently have seizures and delayed language acquisition followed by a rapid decline in motor ,language, cognitive, and visual function over a period of 4 to 6 years and death by early adolescence. There has been no approved therapy for this disorder.

Natural-history cohorts of children with CLN2 disease have shown progressive decline in motor and language function. A database of children with the disease has characterized disease severity and progression with a disease specific clinical rating scale, including motor, language, and visual function, and incorporates the frequency of grand mal seizures. Specific disease genotypes do not consistently correlate with phenotype, although pathologic variants

other than the two most common ones (c. 622C →T nonsense mutation and c. 509-1G → C splice defect) may be associated with an increased probability of a later onset of the disease.

Cerliponase alfa a recombinant pro-enzyme (also called zymogen) form of human TPP1, is an enzyme-replacement therapy that has potential use in patients with CLN2 disease. The administration of enzyme into the ventricular cerebrospinal fluid of young dogs that were spontaneously homozygous for TPP1 deficiency resulted in widespread distribution and uptake in the brain, clearance of lysosomal storage material, preservation of neuronal morphologic features, and a reduction in brain inflammation. The treated dogs also had delayed onset and slower progression of neurologic signs and brain atrophy, preserved cognitive function, and an extended life span in a dose-dependent manner. These findings led to this clinical study of recombinant human TPP1 administered by intraventricular infusion in children with CLN2 disease.

Aim

To study the clinical picture and the manifestations of Neuronal ceroid lipofuscinosis type 2 according to literary sources.

Materials and methods

A theoretical analysis of literary sources and a synthesis of scientific literature for 2015 – 2018 was used.

Results

Table 1 — Score table

Score		**Functional Descriptions**
Motor domain		Language Domain
3	Has grossly normal gait; no prominent ataxia, no pathologic falls	Has apparently normal language that is intelligible and grossly age-appropriate, with no decline noted
2	Has independent gait as defined by ability to walk without support for 10 steps; obvious instability and possibly intermittent falls	Has language that has recognizable abnormalities but includes some intelligible words; may form short sentences to convey concepts, requests, or needs
1	Requires external assistance to walk or can only crawl	Has language that is hard to understand with few intelligible words
0	Can no longer walk or crawl	Has no intelligible words or vocalizations
The primary end point of the study was an aggregate score in the domains for motor and language function on the CLN2 Clinical Rating Scale. Each domain is scored from 0 (no function) to 3 (normal function) for a maximal possible score of 6 for the two domains.		

Treatment

An Ommaya or Rickham ventricular reservoir was surgically implanted, with the reservoir placed under the scalp and the catheter placed in the cerebral lateral ventricle in each patient, with placement confirmed on MRI. Cerliponase alfa was administered by means of intraventricular infusion at a rate of 2.5 ml per hour for 4 hours. An antihistamine drug was administered approximately 30 minutes before each infusion. We conducted a dose-escalation phase in which the study drug was initiated at 30 mg, 100 mg, or 300 mg every 2 weeks, a regimen that was intended to establish an acceptable side-effect Profile.

During the dose-escalation phase, patients received at least two infusions at each dose level 3 patients who started at 30 mg received two to six doses, 3 patients who started at 100 mg received two to five doses, and 4 patients who started at 300 mg received one to three doses. This phase was followed by a 48-week period in which the patients received a stable dose of 300 mg every 2 weeks.

Discussion

In a small group of children with CLN2 disease who were between the ages of 3 and 16 years, the rate of clinical decline was lower among those who received intraventricular infusion of cerliponase alfa than among historical controls. The study was designed as an open-

label, singlegroup study and an extension study. A statistical comparison with a historical control group (including patient-level matching and covariate adjustments) was used to control for possible confounders. A treatment benefit was shown in the efficacy population over a period of at least 96 weeks, although the treatment period was longer for most patients at the time of the data cutoff (median, 116 weeks; range, 96 to 145). All 23 patients in the efficacy population continued in the extension study. Among the treated patients, the annual rate of loss of total gray-matter volume during a 96-week period was 6.7 %, with larger decreases seen during the first year of treatment than during the second year.

Intraventricular administration maximizes delivery of cerliponase alfa to the central nervous system and may reduce the risk of immune mediated adverse events that have been associated with systemic enzyme-replacement therapy. Serious adverse events reflected treatment with exogenous protein into the ventricular system and complications from the intraventricular device. Three serious device-related infections occurred in two patients. Both patients continued therapy after removal of the intraventricular device, treatment with antibiotics, and subsequent replacement of the device, but treatment with cerliponase alfa was delayed. Serious adverse events also included device leakage and hypersensitivity reactions. Further study is required to determine whether intraventricular enzyme replacement treatment is appropriate in other lysosomal storage disorders that have manifestations in the central nervous system.

Conclusion

Intraventricular administration of cerliponase alfa every 2 weeks at a dose of 300 mg in children with CLN2 disease resulted in a slower rate of decline in motor and language function than that in historical controls. The potential uses of intraventricular cerliponase alfa to prevent the onset of symptoms in young patients and to delay or prevent changes in vision warrant further study. Intraventricular enzyme replacement therapy was associated with devicerelated complications, including grade 3 infection, leakage, and an increased white-cell count in cerebrospinal fluid in half the patients.

УДК 616-06

КЛИНИКО-ЛАБОРАТОРНЫЕ ОСОБЕННОСТИ ОСТРЫХ ФОРМ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА У ПАЦИЕНТОВ С ИШЕМИЧЕСКИМ ИНФАРКТОМ ГОЛОВНОГО МОЗГА

Антипина Е. О.

Научный руководитель: ассистент *А. Н. Алексеюк*

Учреждение образования
«Гродненский государственный медицинский университет»
г. Гродно, Республика Беларусь

Введение

Острые цереброваскулярные заболевания относятся к числу наиболее актуальных проблем современной медицины, поскольку они оказывают существенное влияние на такие важные демографические показатели, как заболеваемость и смертность, а также являются одной из основных причин длительной инвалидизации. В настоящее время инсульты, согласно мировой статистике, занимают третье место среди причин смерти населения после сердечно-сосудистых и онкологических заболеваний. Преобладающей формой инсульта является ишемический инфаркт головного мозга (ИИГМ). Течение постинсультного периода может осложняться развитием коронарных катастроф, включая тяжелый инфаркт миокарда (ИМ). Это обстоятельство ставит перед врачом необходимость изучения и своевременного выявления ишемической болезни сердца (ИБС) и