SEMMELWEIS EGYETEM

Általános Orvostudományi Kar

Genomikai Medicina és Ritka Intézete
Igazgató: Prof. Dr. Molnár Mária Judit
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TV
DOB: 1991
Admission: 2022.03.03.
Discharge: 2022.03.12.

Medical history:
She had no major illnesses in his childhood and had a normal developmental milestones chart. In 2008, she was treated several times for earache/ ear canal infection, but his hearing was intact. Around 2010, he was operated on for a right-sided ureteral stricture. Since 2010, she is very thin, unable to gain weight, and occasionally had episodes of vomiting. Currently has 37 kgs. In 2010, during a gastroscopy, atrophic duodenal mucosa and gastritis were seen. An elevated intraepithelial lymphocyte count was confirmed in the duodenal biopsy. In 2017, she started to have hearing loss, which progressively worsened. She was given a hearing aid, but his hearing was not perfect either. In April 2021, following COVID vaccinations, accompanied by severe migraine headaches, her hearing was completely lost and since then she has not been able to hear in either ear. At the same time, she was confirmed to have extensive nasal polyposis, pansinusitis and fungal otitis externa (suspected to be related to hearing aid use). Her hearing loss was considered to be of neural origin. 07.10.2021 internal ear MRI: no abnormalities were found in the angle of the cerebellar bridge, in the area of the internal auditory canals. Extensive white matter abnormalities were seen in supratentorial white matter.
Family history: Her mother and sister have vision problems. Maternal grandmother has thyroid disease, maternal grandfather's larynx cc. There was no family history of DM, epilepsy, short stature, gastrointestinal disorders, or hearing problems.

Current complaints: Due to increasing weight loss, cyclical vomiting episodes and deafness, the patient was suspected to be diagnosed with MNGIE, and was admitted to our inpatient station for investigation and differential diagnosis.
Currently, there are no novum complaints, he mentions intermittent abdominal pain.

Physical examination:
Cachectic appearance, Weight: 37 kg, Height: 168 cm BMI 13.11. Above the right scapula cherry size lipoma. Above the right crista iliaca a 2x1.5 cm cafe-au-lait spot. In the primary gaze (looking straight ahead) the right eye is turned out and down (skew deviation), right side superior rectus and medial rectus palsy, ptosis is also observes at this eye (incomplete right-sided oculomotor palsy), on the left side is also present a vertical gaze palsy, and medial rectus palsy. Able to convergence. No nystagmus or diplopia, despite the disconjugated eye movements. Bilateral anacusis. The pharyngeal and soft palate reflexes are very brisk. Muscle trophy corresponds to nutrition. Normotonia throughout the body. Muscle strength was maintained throughout the body. Muscle stretch reflexes throughout the body are ¼ or weaker, equal. Pyramidal signs are negative. No sensory deficiency in the limbs and trunk, maintained for all qualities. Eudiadochokinesis. Accurate cerebellar tests. Stable in Romberg position. Gait is smooth, steady, and within normal limits. During gait normal contralateral synkinesis.

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Blind-gait holds direction. Bárány's test no lateralisation. Speech assesment: fluency, expression is good, comprehension and repetition cannot be tested due to deafness, she communicates well both in writing and orally. Patient has no urinary or bowel complaints. Appropriate mood and affect. Awake, alert and oriented. No visual or auditory hallucinations. VAS: 1/10 (abdominal pain). Newcastle Mitochondrial Adult Scale (NMDAS): 35 points.

Investigations:

CBC: Basophil granulocyte 0.7 %, GFR normal, Uric acid 275 umol/l (ref:154-357), GOT (ASAT) 25 U/l, RNS Pol. AB, Antinuklear AB 1:40 / 1:160 negative, Antinuclear AB pattern negatve, Centromer AB, PCNA AB, Ku AB, P Ribosomal AB, Cytoplasmic AB Cytosceleton marker AB, Anti-chromatin antibodies, anti-SSA/Ro AB negative with ELISA

Barium swallow test-radiography: the contrast material enters the significantly enlarged, residue-filled stomach, the lower pole of which reaches the pelvis. The stomach wall shows hypoperistalsis, gastroparesis. After the patient was placed on the right side, gastric emptying towards the duodenum began to a small extent, however, the contrast material regurgitated towards the stomach.

Brain MRI: diffusely abnormal brain white matter (increased FLAIR or T2-weighted signal) changes bilateral, symmetric ENG: moderately severe length-dependent sensori-motor demyelinating polyneuropathy with axonal loss.

Stem cell transplantation team: the patient was referred to Dr. Gergely Kriván due to the indication for stem cell transplantation, however, the transplantation team not supported the transplant.

Medication: iv Pabrinex (500ml Rindex5, 1amp SoluvitN, 5amp B1 50mg, 2amp B6 25mg, 1 amp Cvitamin 500mg)

Diagnosis: Obs. ad Mitochondrial Neuro-GastroIntesinalis Encephalomyopathia (MNGIE) - Leukoencephalopathy - Gastroparesis - Cachexia - Anacusis -Sensomotor Polyneuropathy.

Epicrisis: In the background of the disease, which started in young adulthood (at the age of 24), with severe weight loss, ophthalmoparesis, cyclic vomiting syndrome, deafness, diffuse white matter lesion, sensorimotor polyneuropathy we suspected MNGIE syndrome. The lactate stress test confirmed an aerobic metabolism disorder. A swallowing X-ray examination described gastroparesis. Based on the clinical symptoms and examination findings, the existence of MNGIE (Mitochondrial Neuro-GastroIntestinal Encephalomyopathy) is probable. The genetic testing found compound heterozygous rare variants in the TMYP gene: 1) c.866A>C | p.Glu289Ala is pathogenic and 2) c.457G>A | p.Gly153Ser likely pathogenic variants, which support MNGIE disease. MNGIE is a multisystemic disorder which requires cooperation among multiple specialties including neurology, clinical genetics, nutrition, gastroenterology, pain management, psychiatry.

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No drug treatment is available for the disease. Allogeneic haematopoietic stem cell transplantation or liver transplantation may be beneficial. After careful consideration, the bone marrow transplant team has not recommended a bone marrow transplant due to an unfavorable risk/benefit ratio. Therefore, with the patient's consent, an ASAP CPMS consultation was done on the usefulness of liver transplantation and the experience with bone marrow transplantation. As a result of the consultation, a liver transplant was recommended. We therefore contacted the liver transplant team. The case was presented to the liver transplantation team in the framework of a case report. Relevant literature data were electronically sent to the liver transplantation team.
Due to cachectic state, the patient received parenteral vitamin infusion, physical therapy and benefited from dietetic counseling. In case of diarrhea the supplements should be diluted with water.
Due to hypoacusis, the possibility of a cochlear implant was raised by the oto.rhino-laryngologist and further tests were indicated..
The possibility of peritoneal dialysis was raised as a bridge therapy before the liver transplantation. We discussed this with the patient and the head of the Semmelweis Dialysis Center. In agreement with the patient, we initiated the preparation for peritoneal dialysis.
The patient was transferred to the Department of Surgery, Transplantation and Gastroenterology, Semmelweis University for the peritoneal dyalisis chateter placement. Dr. Kevei will inform the patient about the tasks related to peritoneal dialysis.

CBC and iron level chek-up in 2 weeks is recommended, for this investigation the GPs help is asked.

Recommendations: - Vitamin B komplex 1x, Myoqinon Q10 2x100mg, C vitamin 1000mg, Vitamin D3 3000NE, Neoferrofol gamma 1x. Fresubin 2x 200 ml.

In our department, a follow-up examination is recommended at 05.06.2023.

The patient has been informed in written and smart device application about his medical condition, the proposed tests and interventions, the possible benefits and risks of having or not having them, the planned dates of the tests and interventions, his right to decide about the proposed tests and interventions, the possible alternative procedures and methods, the course of treatment and the expected outcome, further care, the proposed lifestyle.

Budapest, 12/03/2022