SEMMELWEIS EGYETEM

Általános Orvostudományi Kar

Genomikai Medicina és Ritka Intézete
Igazgató: Prof. Dr. Molnár Mária Judit
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SZ
DOB:1983
Admission: 2022.04.10.
Discharge: 2022. 04.18.

Medical history

The 39 yo patient lives in Poltava, Ukraine. At the age of 24, she had a cardiac arrhythmia and was diagnosed with preexcitation syndrome, which led to an ablation. He broke his ankle 8 years ago, since then his gait has become more unsteady. Before that he had an active life, no coordination problems. After that it was noticed that his left corner of the mouth is lower, he feels more tired. He sometimes gets dizzy. His speech has become slower, stuttered, and his articulation has deteriorated. He also complains about frequent hip pain for about 2 years.

Family history: No similar disease affecting the vestibular system was noticed in the family. His mother had a hysterectomy for myoma and an opus for invasive ductal carcinoma of the left breast, in addition she has multiple lipomatosis progressive in size throughout the body. His father was diagnosed with gastric cancer in 2002, for which he received radio-chemotherapy, and has been asymptomatic for many years. Maternal grandparents also have a history of cumulative cancer. His paternal great-grandfather was blinded at a young age, probably due to an accident. Has two unaffected brothers. No children yet.

Previous investigations:

Brain MRI found moderate cerebellar atrophy. He was treated with ceftriaxone due to suspicion of Borrelia (Borrelia IgM positive). Abdominal CT revealed a hepatic haemangioma. His ceruloplasmin level was slightly decreased. HBV, HCV, HIV negative. Ophthalmological examination revealed no abnormalities. Electrophysiological examination confirmed bilateral peroneal nerve axonal neuropathy. Previous genetic testing for spinocerebellar ataxia (SCA 1,2,3,6,7) was performed and was negative, so the pathogenic role of these genes in the disease can be dismissed. Because of the negativity of these genes, ATM gene testing was an option (due to slightly higher AFP values). The cervical spine MRI showed discopathy at the level of C2-6 roots, no signs of root compression or spinal space narrowing. Suspicion of haemangioma vertebrae in Th.1. and Th. 2. No evidence of aerobic metabolic disturbance on lactate stress test. During the time his writing has deteriorated, his legs tend to hurt occasionally, in the distal part of the legs, this tends to be worse in the morning and then improves as the day progresses. His speech shows fluctuating quality, sometimes better, other times less articulatory.
Smoking, alcohol: denied
CAVE!: unknown

Current complaints:

The patient was admitted for a long history of progressive coordination complaints, and further investigations. His current status showed cerebellar symptoms (gait and limb ataxia, nystagmus, dysdiadochokinesis, dysarthria). Her routine laboratory showed hypercholesterolemia, hyperuricemia, mildly elevated CK (394 U/l) and minimally elevated AFP levels. For a few months he complaints numbness in the left IV-V. fingers.

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Physical examination:

Well developed, hydrated and nourished. Weight: 90 kg, Height: 185 cm. No internal, visceral, cardiac abnormalities. No telangiectasias are seen on skin. Symmetric visual fields. Extraocular muscle movements intact, pupils equally reactive to light. Their direct and consensual light response is retained. On smooth pursuit test on side on side gaze diplopia occurs. Horizontal nystagmus. Mild facial asymmetry, peripheral left sided facial palsy. Dysarthria. Muscle trophy corresponds to nutrition. Normotonia throughout the body. Muscle strength was maintained throughout the body. Muscle stretch reflexes throughout the body are 2/4 equal. Gait ataxia. In the Romberg position unsteadiness is present, blind gait unsteady. He also had limbataxia. The writing test shows coordination problems. No retropulsion. Mild intention tremor is seen bilateral. Superficial and deep sensations are retained. Patient has no urinary or bowel complaints. Psychologically alert, orderly, conventional. Retained cognitive functions. Speech assessment: fluency, comprehension, repetition is good. Frontal release signs negative. Appropriate mood and affect. Awake, alert and oriented. No visual or auditory hallucinations. SARA score: 4-3-1-2-1-1-1-1-1-1-2-2.

Invastigations: mildly elevated AFP 9,3 ng/ml (Norm: < 8,8), CBC within normal ranges.

2022.04.12: CSF examination: The patient was properly informed about the need for the test, its methodology and possible complications. The patient has given written informed consent for the test. Lumbar puncture confirmed minor VLG damage.

Diagnosis: Ataxia teleangiectasia (genetically proved)

Epicrisis:
The 39 yo. male patient has a 12 years long history of progressive coordination complaints. He is currently admitted to our department for deterioration, genetic counseling and further laboratory tests. Currently beside the cerebellar complaints he also complains about numbness in the left IV-V. fingers. With regard to numbness of the hands ENG examination was performed, which suggested lower limb radiculopathy, but no lesion on the left ulnar area. The CSF analysis showed minor VLG damage.
During genetic testing we confirmed the presence of two pathogenic mutations in ATM gene. The segregation study of the parents confirmed that the two variants are carried in a trans position, so the compound heterozygous status is confirmed. Based on the above, the patient is diagnosed with ataxia telangiectasia (OMIM:AT; # 208900) .
The ataxia telenagiectasia is characterized by cerebellar ataxia, telangiectases, immune defects, and a predisposition to malignancy. In this particular genetic disorder the body's DNA repair mechanisms are damaged, which is why the patients diagnosed with this condition may be more prone to cancer than the general population. AT cells are abnormally sensitive to ionizing radiation, and abnormally resistant to inhibition of DNA synthesis by ionizing radiation.

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Reccomendations:

Multidisciplinary management that emphasizes monitoring of recurrent infection, neurological symptoms, immunodeficiency. In every 6 months neurological follow-up, regular physical therapy to improve or maintain the coordination, and to reduce the risk for contractures and scoliosis.

For comprehensive immunologic evaluation the patient is transferred to the Department of Internal Medicine and Oncology, to immunological evaluation (Dr. Jakab László).

Annual CBC, lactate dehydrogenase (LDH), and comprehensive metabolic panel measurement should be performed. Regular pulmonary function testing. Live vaccines are contraindicated for patients with AT due to partial combined immunodeficiency.

Because of the increased sensitivity of A-T cells, use of ionizing radiation and some chemotherapeutic agents requires careful monitoring. Alkylating agents and epipodophyllotoxins should be avoided; methotrexate doses should be reduced. The patient should avoid frequent sun exposure, only with UV protection (50+ SPF), should avoid ionizing radiation (CT of excessive radiological investigations). These raise the possibility of melanomas. Yearly based, careful dermatological screening.

Careful attention for using general anesthesia, because due to ataxia and coordination problems, there is an increased risk of aspiration.

We recommend genetic counseling for all the risk relatives in the family. The patients with heterozygous ATM variants have also a mildly elevated risk for breast cancer.

He is expected to be followed up as an outpatient in his country. The patient was referred to Department of Medical Genetics, Kharkiv National Medical University (Address: Nezalezhnosti, av., 13, Kharkiv, Phone +38 057 705 05 16). If needed in our department is open for further consultation, a follow-up examination is recommended every 6 months within the framework of a telemedicine consultation.

After your hospitalization, please see your GP as soon as possible to present your final report.

The patient has been informed orally 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, 18/04/2022.