CLINICAL CASE OF A PATIENT WITH PROGRESSIVE SUPRANUCLEAR PALSY – FROM SYMPTOM TO DIAGNOSIS

Zh. Dimova, V. Boyadzhieva, S. Emin, N. Stoilov

Rheumatology department, UMHAT "Sv. Ivan Rilski" – Sofia, Bulgaria

Abstract. *Progressive supranuclear palsy (PSP) is a neurodegenerative disease classified among the atypical forms of parkinsonism. PSP is characterized by great variability in the involvement of different areas of the central nervous system (CNS). The clinical picture is associated with impaired gait and balance, generalized bradykinesia, visual impairment, dysarthria, dysphagia, pelvic incontinence, dementia and others. We present a clinical case of a 50-year-old woman who, at the end of 2021, was admitted to the Rheumatology department, UMBAL „Sv. Ivan Rilski" – Sofia, due to weakness in the hands, dropping objects, pain in small joints of the hands, disorder in coordination, difficulty walking and frequent stumbling, slurred speech, tremors involving both hands (more pronounced on the right), memory impairment, pelvic incontinence and hair loss. The clinical case is very indicative of the long journey that a patient with progressive supranuclear palsy takes before being correctly diagnosed.*

Key words: *progressive supranuclear palsy, atypical forms of parkinsonism, MRI*

Introduction

Progressive supranuclear palsy (PSP) is a rare and rapidly progressive neurodegenerative disease that is classified among the atypical forms of parkinsonism. More than half a century ago, Steele, Richardson, and Olszewsk first described the clinicopathological nature of PSP. Until then, patients were misdiagnosed with vascular parkinsonism or Parkinson's disease [1].

PSP is a complex disease for which no cure or disease-modifying therapies have yet been discovered and which can only be definitively confirmed at autopsy [2].

The incidence of progressive supranuclear palsy varies around 5-6 cases per 100,000 people, with only 1.5 per 100,000 being correctly diagnosed. By comparison, the incidence of Parkinson's disease is 150-200 cases per 100,000. The most important among the genetic risk factors for the development of PSP is the presence of the H1-haplotype of the MART gene, which encodes the „tau" protein [1].

Progressive supranuclear palsy is characterized by great variability in the involvement of different areas of the central nervous system (CNS). Disturbances in dopaminergic and cholinergic pathways in different areas of the CNS, as well as changes in neurotransmitters, are among the most common changes in PSP. Although disturbances in the basal ganglia and cortex are important in PSP, the loss of structures in the brainstem is pathognomonic of this disease.

The clinical picture in PSP is characterized by impaired gait and balance, generalized bradykinesia, impaired vision, dysarthria, dysphagia, pelvic incontinence, dementia, and others. Treatment of progressive supranuclear palsy remains symptomatic for now. Levodopa treatment, which is used in patients with Parkinson's disease, shows effectiveness in terms of muscle rigidity and bradykinesia. In the presence of blepharospasm, the application of Botulinum toxin is recommended [1].

There are currently ongoing clinical trials that target the abnormal aggregation of the „tau" protein through various mechanisms, including immunotherapy and gene therapy [2].

Clinical case

It concerns a 50-year-old Caucasian woman, who at the end of 2021 was hospitalized in the Rheumatology department, „Sv. Ivan Rilski" UMHAT – Sofia, due to muscle weakness in the upper limbs. The patient reports dropping objects, difficulty gripping, arthralgia in the small joints of the hands, tremor (more pronounced on the right). Over the past 3 months, there has been progressive incoordination, difficulty walking with frequent stumbling, slurred speech, tremor involving both hands (but more pronounced on the right), memory impairment, pelvic incontinence and hair loss. Complaints date back to the summer of 2020, debuting with deterioration of vision (change in the shape of objects). In January 2021, the patient

noticed a worsening of the tremor, which involved both hands. In February 2021, an MRI of the brain was performed, from which old gliotic changes of a vascular nature were established. Suspicious myogenic changes in the upper and lower limbs were suspected from the performed ENMG. After hospitalization in a neurology department, the patient was diagnosed with Multiple Sclerosis (MS), treated with CS – with an unsatisfactory effect. Due to worsening in her condition, the patient was hospitalized in another neurological department, where the diagnosis of MS was rejected and she was discharged with a diagnosis of Parkinson's disease. Therapy with Madopar and Prampexole was started for 1 month – initially with minimal improvement – later – complete absence of effect. SPECT was performed – with the conclusion that there was no evidence of loss of dopaminergic neurons in the striatum. The diagnosis of Parkinson's disease was rejected and the patient was referred for consultation with a rheumatologist. Due to the progressive muscle weakness, in the clinic of Rheumatology, immunological tests were carried out in the direction of Systemic connective tissue disease – ANA titer 1:160 was established, with a negative ANA immunoblot and Myositis immunoblot, ANCA – negative, Antiphospholipid package – negative. The patient is diagnosed with congenital thrombophilia – Heterozygous carrier for MTHF and heterozygous carrier for PAI, 4G/5G mutation. Abdominal ultrasonography showed pronounced liver fibrosis, which is why Wilson's disease was suspected and was recommended testing of the serum levels of Cu. There was made a consultation with an imaging specialist, who expressed the opinion that the changes in the brainstem from the MRI of the brain were most consistent with progressive supranuclear palsy. The patient was referred to the Clinic for Nervous Diseases, where the diagnosis was confirmed and treatment was started.

Laboratory results: Hematological and biochemical indicators – within reference limits, ESR – 5, CRP – 0.70, Urine – normal, Cu – within reference limits.

Immunological results: ANA – titer 1:160; ANA immunoblot – negative; Myositis immunoblot – negative; ANCA – negative; Antiphospholipid package – negative.

Ultrasound of abdominal organs: Diffuse parenchymal process in the liver, normodynamic portal blood flow, no steatosis – stages of fibrosis F3. Wilson's disease must be ruled out. Facial X-ray of lungs and heart – b.o., Facial X-ray of wrists with fingers – mildly narrowed DIFJ.

Brain MRI – Irregularly shaped or punctate areas of altered signal intensity are visualized supratentorially bilaterally in the subcortical white matter. The findings are without mass effect and without restriction of the diffusion of water molecules. The ventricular system is symmetrically dilated as in internal nonocclusive hydrocephalus. The subarachnoid spaces and basal cisterns are dilated. A reduction in the volume of the mesencephalon is visualized, which has convex upper contours, forming an image of the „Humming bird sign" type. A thinning of the superior cerebellar peduncles is visualized.

Conclusion: MR data for old gliotic changes of a vascular nature. MR evidence of cerebral atrophy. The described changes in the brain stem are suspicious for Progressive supranuclear palsy.

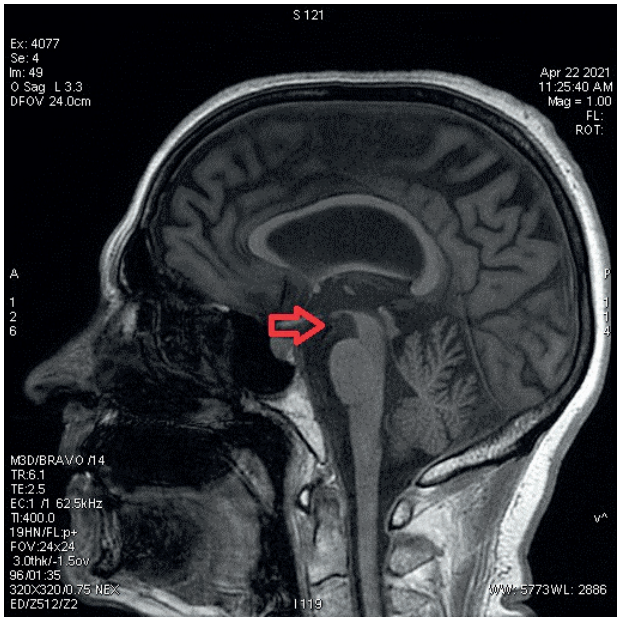

Fig. 1. Humming bird sign

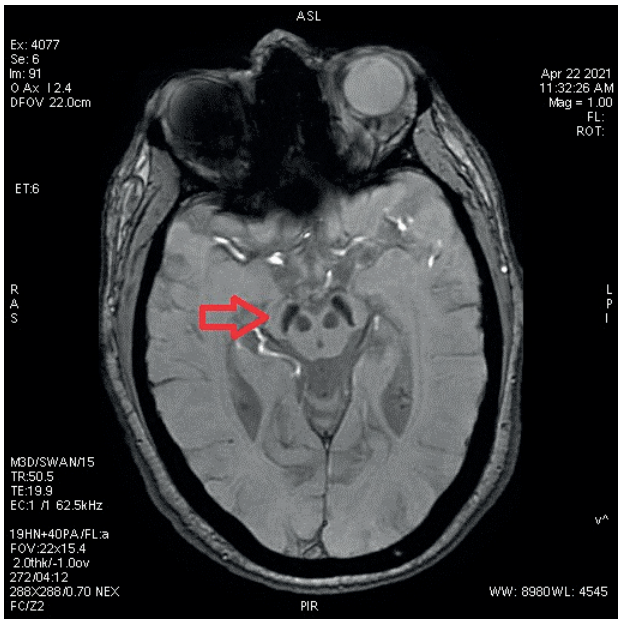

Fig. 2. Mickey mouse sign

Discussion

The present clinical case is indicative of the long journey that a patient with progressive supranuclear palsy takes before being correctly diagnosed. In clinical practice, the only way to make the correct diagnosis of these patients is on the basis of history, neurological status and correct reading of MRI of the brain [1]. MRI examination is the best diagnostic method for PSP, the most characteristic being the „Hummingbird sign“ and „Mickey Mouse sign“ [3, 4]. „Hummingbird sign“ represents midbrain atrophy. It is also known as the „penguin sign“ and is used to distinguish PSP from Parkinson‘s disease and multisystem atrophy (MSA) [5, 6]. The magnetic resonance parkinsonism index, defined as the ratio of the area of the midbrain to the area of the pons, is another suitable method for the diagnosis of PSP [7, 8]. „Mickey Mouse sign“, also called „Morning glory sign“ describes the image of increased lateral concavity of the midbrain, as a result of atrophy [9, 10, 11].

PSP is a rare neurodegenerative disease affecting patients over 40 years of age, in about 55% of cases male. The differential diagnostic process is an important and difficult stage in this group of patients, due to the heterogeneity of symptoms. It is necessary to rule out other diseases with neurological deficits, including MS, cerebrovasculitis (isolated or in the context of SVT), Wilson‘s disease, recent encephalitis, and others. Life expectancy in these patients is about 7 years, with a delay in diagnosis ranging from about 3-4 years [1].

Библиография / References

1. Golbe L. Progressive Supranuclear Palsy, Seminars in Neurology, 2014, 34(02), 151-159.
2. Coughlin DG, Litvan I. Progressive supranuclear palsy: advances in diagnosis and management. Parkinsonism Related Dis. 2020,73,105-116.
3. Imaging and atypical parkinsonism – ACNR | Paper & Online Neurology Journal ACNR | Paper & Online Neurology Journal. Available: https://www.acnr.co.uk/2015/01/imaging-and-atypical-parkinsonism/ [Accessed 28 Aug 2022].
4. Massey LA, Micallef C, Paviour DC, et al. Conventional magnetic resonance imaging in confirmed progressive supranuclear palsy and multiple system atrophy 2012, Mov. Disord. 27(14);1754-1762.
5. Groschel K, Kastrup A, Litvan I, Schulz JB. Penguins and hummingbirds: midbrain atrophy in progressive supranuclear palsy. Neurology. 2006;66(6):949-50.
6. Graber JJ, Staudinger R. Teaching NeuroImages: “Penguin” or “hummingbird” sign and midbrain atrophy in progressive supranuclear palsy. Neurology. 2009;72(17):e81.
7. Berg D, Steinberger JD, Warren OC et al. Milestones in magnetic resonance imaging and transcranial sonography of movement disorders. Mov Disord. 2011;26(6):979-92.
8. Pandey S. Hummingbird sign in progressive supranuclear palsy disease. J Res Med Sci 2012; 17:197-198.
9. Adachi M, Kawanami T, Ohshima H, et al. Morning glorysign: a particular MR finding in progressive supranuclear palsy. Magn Reson Med Sci 2004; 3:125-132.
10. Mueller Ch, Hussl A, Krismer F et al. The diagnostic accuracy of the hummingbird and morning glory sign in patients with neurodegenerative parkinsonism. Parkinsonism Related Dis. 201854; 90-94. https://doi.org/10.1016/j.parkreldis.2018.04.005.
11. Kato N, Arai K, Hattori T. Study of the rostral midbrain atrophy in progressive supranuclear palsy. J Neurol Sci. 2003. 210(1-2), 57-60.

Постъпил за печат: 30.08.2022 г.

Submitted: 30.08.2022

✉ *Адрес за кореспонденция:*
Д-р Владимира Бояджиева, дм
e-mail: vladimira.boyadzhieva@gmail.com

✉ *Correspondence address:*
Vladimira Boyadzhieva, MD
e-mail: vladimira.boyadzhieva@gmail.com