World Academy of Science, Engineering and Technology
International Journal of Psychological and Behavioral Sciences
Vol:14, No:9, 2020

Multidisciplinary Approach to Diagnosis of Primary Progressive Aphasia in a Younger Middle Aged Patient

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***Abstract*—**Primary progressive aphasia (PPA) is a neurodegenerative disease similar to frontotemporal and semantic dementia, while having a different clinical image and anatomic pathology topography. Nonetheless, they are often included under an umbrella term: frontotemporal lobar degeneration (FTLD). In the study, examples of diagnosing PPA are presented through the multidisciplinary lens of specialists from different fields (neurologists, psychiatrists, clinical speech therapists, clinical neuropsychologists and others) using a variety of diagnostic tools such as MR, PET/CT, genetic screening and neuropsychological and logopedic methods. Thanks to that, specialists can get a better and clearer understanding of PPA diagnosis. The study summarizes the concrete procedures and results of different specialists while diagnosing PPA in a patient of younger middle age and illustrates the importance of multidisciplinary approach to differential diagnosis of PPA.

***Keywords*—**Primary progressive aphasia, etiology, diagnosis, younger middle age.

I. Introduction

THERE are variety of neurodegenrative diseases and PPA is one of them. "It is characterized by a progressive speech impairment, affecting first the efferent motoric and later also the sensory part. PPA often ends with severe dementia syndrome, akinesis and mutism [1]". From the perspective of theoretical categorization [2], PPA falls under the FTLD along with frontotemporal and semantic dementias, or sometimes under the category of Pick complex.

It is important to emphasize the difference in the clinical image and pathological anatomical topography [3]. Topographically, PPA is characterized by asymmetrical brain atrophy, mostly of the dominant hemisphere [1], [4]. For PPA diagnosis, progressive speech impairment is often necessary. However, during the disorder also other symptomatology suggesting frontal lobe dysfunction can be registered, for example, symptoms of prefrontal syndrome or mood disorders [2], [3]. To be able to diagnose PPA, only speech impairment is insufficient, there must be a progressive aspect to it [3]. Increased noticeability of disorder by others is also due to the aphasic stuttering or incomplete sentences.

Apart from other symptoms, there is also increased usage of neologisms, poor vocabulary or disturbance of lexia, graphia and counting, also due to the progression of disorder of phatic functions. According to [5], the difference in diagnosing is based also on morphology of affected neurons and glia cells. They write that "Pick type" is characterized mostly by gliosis of white and grey matter and by presence of achromatic edematous neurons with frequent inclusion illustrating Tau-protein immunopositivity reflecting precisely the Pick bodies. On the other hand, Cortico-Basal Dementia (CBD) contains only achromatic edematous neurons without Pick bodies. Frontal Lobe Degeneration Type (FLDT) is characterized by extensive death of pyramidal cells in frontotemporal isocortex with microvacuolization and mild gliosis. However, according to [6], the important factor is the type of protein occurring in the intraneuronal inclusions and also that the clinical image is determined by macroscopic distribution of pathology regardless of histopathological type [5].

In the diagnostic process, however, crucial factor is the progressive speech impairment, disturbed spontaneous speech production or the ability to understand speech and label things correctly. In effective diagnosing it is inevitable that patients undergo also neurological, logopedic and neuropsychological examination. In conjunction with these assessments, also CT or MRI results are considered to exclude focal lesions correlating with other speech disorders. Equally important is also a genetic screening to investigate mutations of protein gene associated with the occurrence of Pick Complex or PPA.

In the literature, we meet different subtypes of PPA [12], [13], recording the various clinical pathological correlations of these specific PPA phenotypes. The incidence and prevalence of PPAs is often not discussed in the literature and the data itself are rather informative, mostly derived from FTLD data. In literature [12], however, we find that the prevalence of FTLD is about 2.7 to 15 cases per 100,000 inhabitants, while the incidence of FTLD alone is about 2.2-3.5 per 100,000 inhabitants per year. It is further noted that of these, about 20-40% of the FTLD cases are also clinically PPA cases.

Looking at PPAs in terms of age, we see a wide range (20-82 years), and in most cases the average onset of illness is 55-60 years. In the casuistry is presented a patient who, although belonging to this broad group, nevertheless had the onset of the disease in him before the mean of the disease itself [12].

In the context of terminology, the PPAs also underwent a number of changes, the amendments themselves relating in particular to their more detailed specification, reflecting in particular the subtypes of PPAs. The description of the PPAs was already given at the 20th anniversary [14], during which time the first ever PPA capturing through the description of

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the PPAs' cases took place. In this publication [14], we learn more about the fact that the speech disorder itself has been manifested in patients without any memory disorder or other symptoms similar to dementia. In view of the wider variability in the clinical picture of PPA patients, several types of PPA have been described on the basis of a specific observation, which has been broken down into different subtypes of PPA.

Although there may be similarities between subtypes in some characteristics and many authors describe [1]-[5] them in similar styles, the division itself mainly concerns a certain dominant feature which highlights the deficit itself. However, in the literature [13]-[15] we have the possibility to register general descriptive criteria for PPAs.

The first step is the presence of a newly emerging and progressive speech disorder that occurs in the assessment of language functions in one or more areas. This may include, for example, the following areas:

- disorders of grammatical sentence structure in speech pro duction,
- disorders of word search in a mental lexicon during speaking,
- disorders of the nominative function of speech (problems in naming objects, activities),
- disorders of comprehension of words and sentences,
- written speech disorders (impaired writing and/or reading),
- disorders of repeating words, sentences. An isolated word articulation disorder is not a sufficient criterion for PPA designation.

Furthermore, it may be an area for which it is typical that in the initial stage, episodic memory, executive functions, or visual-spatial abilities documented by examination or anamnesis are relatively preserved. In addition, it is essential that non-neurodegenerative pathologies are excluded, specifically in the case of imaging methods. Some authors [14], [15] perceive the PPAs as a pathological diagnosis and, over time, this narrow threshold perception has not proved to be an effective. In the past, at the implicit level, it was assumed that the PPA had a pathology other than AD, although some patients, particularly in the initial phase of the disease, showed some type of PPA in the pathological diagnosis of AD. In a summary of multiple outcomes [15], it was noted that there is a specific association between clinical PPA syndrome and the neuropathological syndrome in 50% of patients with PPA.

In the nonfluent/agrammatic variant of PPA, taupositive pathology, including Pick's bodies, has been reported in most cases. Within the semantic variant, inclusions with TDP-43 protein deposits had more than 2/3 cases. In the case of speech-induced PPA, Alzheimer's pathology appeared as the main basis in more than half of the patients.

In the following paragraphs, we describe in more detail the different variants of the PPAs and describe the main divisional elements [16]. In our presented casuistry, the patient had a nonfluent/agrammatic variant of PPA.

For the nonfluent/agramatic variant of PPA, it is typical that symptoms related to speech itself are very similar to non-fluent aphasia, which is typical of vascular aetiology such as Broca's aphasia. Among the main symptoms of this subtype of PPA, progressive symptoms are included, with at least one of the symptoms present at the speech level (anaemia, phonemic paraphasia) or at the morphologic syntacation (agramatism), as part of the inconsistency of speech. However, anaemia in these patients is not related to the impairment of the name of the isolated words, which is actually reflected in practice by the absence of a semantic deficit. In this subtype of PPA, we notice that the patient can imagine a word he wants to say out loud, but it is very difficult for him to say it and so he often begins to describe it as, for example, a function, a characteristic of a person, or a shape of a person. However, as far as the use of verbal frequency is concerned, it is maintained in the patient. In case of impaired ability to decode the word-to-word association, this symptom may be observed in the patient during the first stages of the illness.

Language deficits in verbal expression themselves can also appear in written form. We register that patients have a problem with reading, especially when reading more demanding words aloud in which we perceive paralexies - replacements of sounds. When writing to patients with this subtype, PPA produces short sentences, agramatic with a number of errors, which relate mainly to letter substitutions. Within PPA, however, it also recognizes another subtype, which is referred to in the literature [13]-[15] as a semantic variant of PPA.

In contrast to the nonfluent/agramtic variant of PPA, in this case we register that the patient's continuous speech production with impaired comprehension may resemble fluent vascular aphasia of the Wernick type. However, within this subtype of PPA, we register very early onset of disease, which mainly affects semantic memory, and then we register speech disorders. Although patients in this case cannot understand the meaning of the words, they can repeat it after the doctor, and the same principle applies to the reading itself (they use a non-semantic way of reading).

As part of the verbal speech, we see frequent semantic paraphasia, but they often also have a problem with mental lexicones, which also results in frequent anomic pauses. It is typical of this PPA subtype that patients initially have both a well-functioning morphology and syntax, forming phrases that are also grammatically correct but may be irrelevant [17].

Within the PPA, we also meet with the so-called Logopenic variant of PPA, for which it is typical that agramatisms do not appear in the patient's speech and at the same time the patient does not have problems with understanding isolated words. The results of [18] showed that one of the main factors determining the speech therapy variant of PPA is anomic pauses, while patients have problems with naming objects during speech therapy. One of the last criteria [16] indicates that the clinical picture may also resemble vascular-type aphasia in the logopedic variant of PPA.

II. Procedure and Methods

A. Clinical Course

Patient (33) was in care of many specialists (neurologist, neuropsychologist, speech therapist, psychiatrist) for progressing speech impairment in comorbidity with liver failure and cardiovascular problems. First symptoms of speech impairment occurred at the age of 29, but at this time his memory, comprehension and autopsychic and allopsychic orientation were without pathology. At the age of 31 significant intensification of speech impairment occurred with multiple paraphasia and disturbance of mnestic functions. At the age of 33 there is a severe efferent motoric aphasia with disturbance of all parts of speech.

B. Neuropsychological Examination

In the several psychodiagnostics methods WMS-IIIa, WAIS-R, FAB (8), TULIA-AST, FBI (20), MMSE (23) patient scored on the level of mild dementia with agrammatic variant of PPA of the middle severity and mild frontal syndrome with the decrease in ability of abstract thinking and dysexecutive syndrome. Client also displayed a low intelligence (IQ = 70) with better score on performance tasks as compared to the verbal tasks but on both with distinct decrease. Mnestic quotient (MQ = 70) showed better performance on short-term nonverbal than verbal memory, which were worsened in comparison with previous neuropsychological examination.

In general, also lowered ability of abstract thinking and deductive reasoning, poorer concentration and tenacity of attention were registered. In visual stimuli and sentence repetition during all examinations, progressive phonemic paraphasia as well as speech apraxia were present. Also, utilization and compulsive behavior disturbances were registered along with hyperorality.

C. Speech Therapist Examination

Used methods (AST- Arizona Semantic Test, TPO- Test of naming, TPV- test of sentence comprehension, subtests DgAAA- writing and reading) showed the presence of PPA according to the criteria reflecting the expressive and impressive area of speech as well as verbal apraxia [7].

D. Genetic Screening

Mutation of gene E200K was not present, and the polymorphism of prion gene on codon 129 was methionine.

E. Medical Imaging Examination

MR

MR of the brain did not show focal changes as intensity of white and grey matter was appropriate in all weightings. There were no focal changes in diffusion weighted imaging. Cerebrospinal spaces were of appropriate width with slight asymmetry in the width. Corpus callosum was without pathology. MR angiography showed all main brain arteries without pathological changes (Figs. 1, 2).

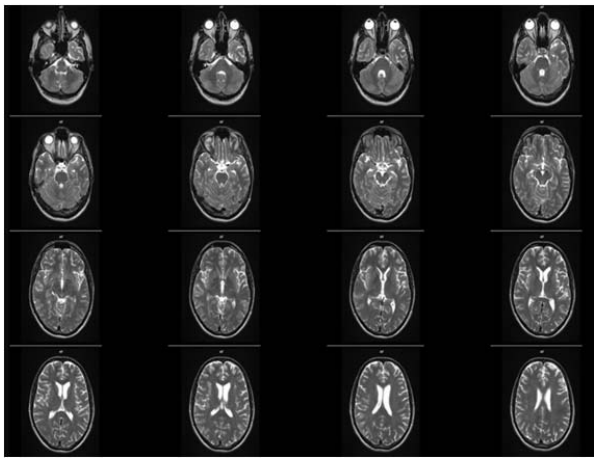

Fig. 1 Complex MR images of brain

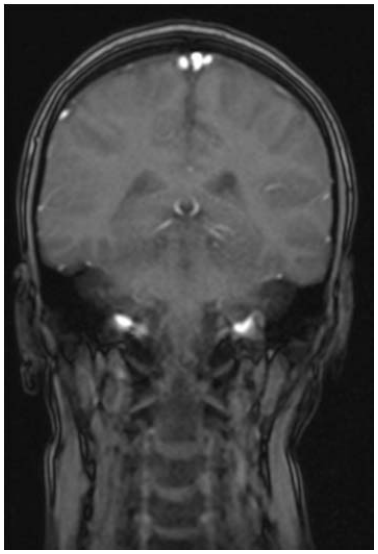

Fig. 2 Special MR image of brain

PET/CT

The results showed decrease in glucose metabolism of cortex, assymetrically to the left frontal to fronto-temporal with the maximal changes in the area of medio-frontal cortex, cingulate gyrus anterior left. Distribution of changes was the closest to the characteristic of PPA-G (nonfulent/aggramatic) variant of PPA.

III. Conclusion

Progressive speech impairment reflecting expressive aphasia should be the first indicator to consider PPA. However, at the early stages, it is oftentimes difficult to set diagnosis as sometimes not even the imaging methods can show focal changes on the brain. For that reason, cooperation of experts with different backgrounds is important to secure precise diagnosis. Apart from that, in the early stages of diagnosing also other ideas about potential disorders can occur, such as Alzheimer's Disease, for which a disturbance of mnestic functions is the most typical, and speech impairment occurs only in the later stages. Considering that PPA is a

neurodegenerative disorder, the treatment is very limited and is mostly focused on supportive treatment in the sense of keeping the patient functional for as long as possible.

IV. Discussion

PPA is a neurodegenerative disorder with progressive character, which from the start only marginally affects cognitive functioning, but in time impairs it significantly. Understanding of speech, spatial imagination or ability to name objects gets impaired substantially. For PPA is typical that during the first two years, speech impairment occurs, but later also visuospatial and mnestic disturbances start as well as apathy and disinhibition. During differential diagnostic examination it is important to consider differences in the onset of individual symptoms, as PPA starts as expressive aphasia and the first problems occur in the search for words, difficulty of naming objects and decreased fluency of speech [8]-[11]. Due to the progression also problems in reproduction and comprehension occur as well as mnestic impairment. On the other hand, during Alzheimer Disease, mnestic impairment occurs first and the speech disturbance only later. Considering [8]-[10], which state that familiar forms of PPA are often connected to the genetic mutation of tau protein gene, the current genetic screening showed that the mutation of E200K gene was not present, while the polymorphism of prion gene on the codon 129 was methionine. Fundamental finding in imaging examination is often asymmetrical brain atrophy in the dominant hemisphere, which was not observed on the initial MR results, which showed just slightly more emphasized subarachnoid spaces fronto-parietally bilaterally. Later conducted PET/CT showed asymmetrical decrease in glucose metabolism in the cortex in the left frontal to fronto-temporal with the maximal changes in the area of medio-frontal cortex and cingulate gyrus in the anterior left, which is typical for PPA-G (nunfluent/aggramatic) variant of PPA. In the paper it was shown that although the diagnosis of PPA is often times very difficult, it is more than important to approach it carefully and with the collaboration of the multidisciplinary team of experts.

Acknowledgment

The author thanks everybody who helped with the study by cooperation in the diagnostic process.

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During his studies he volunteered at the department of child oncology as well as lectured for the UNICEF. He worked as a professional guarantor of the program for application of neuropsychology in the Montessori method in Mexico, Spain, and Africa. Currently, he gives lectures at two Slovak universities and works as a founder of his psychology consulting firm. Most importantly, however, he is a father of two daughters and a happy husband.