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Does this patient have primary progressive aphasia?

■ ABSTRACT

Primary progressive aphasia (PPA) is a distinct clinical entity in which the patient develops language deficits while other cognitive domains remain relatively preserved until late in the course of the illness. The diagnosis can be relatively clear through an appropriate diagnostic approach based on the history and physical examination. There is no cure, but speech therapy is beneficial in this illness.

■ KEY POINTS

The differential diagnosis of PPA includes stroke, mass lesion, and Alzheimer disease. Neuropsychiatric testing is useful to help differentiate the cognitive deficits of various dementing diseases.

Preliminary assessment of language can be done in the office. An example would be to ask the patient to identify geometric shapes, parts of the body, or components of common objects.

Laboratory testing is uninformative in PPA. Electroencephography is normal in 75% of cases, and computed tomography and magnetic resonance imaging are normal in 50%.

AN 81-YEAR-OLD WOMAN presents with complaints of “word-finding problems” and “difficulty finishing sentences” that began approximately 4 years ago. Her daughter states that the patient starts a sentence without difficulty and is fluent to a point, but struggles to find words. Her speech recognition, written language skills, and memory are intact, as is her ability to perform basic and instrumental activities.

Her medical history includes hypertension, esophageal reflux, and mitral valve prolapse. She is a retired nurse, she smoked in the past but does not smoke now, and she rarely consumes alcohol. Her father died of Alzheimer disease at age 86. Her medications include verapamil (eg, Calan), famotidine (Pepcid), and a multivitamin.

Review of systems is notable for vision deficits (corrected with glasses), occasional urge incontinence, and feeling more “melancholy” since her husband’s death 5 months ago.

The entire physical examination results, including vital signs, are within normal limits. On testing of mental status, she scores 30 (of a possible 30) on the Mini-Mental State Examination (MMSE), she can draw a clock face, and she scores 7 (of a possible 17) on the Geriatric Depression Scale (short form), indicating depression. She has difficulty starting sentences and often cannot complete her thoughts. She states “I know what I want to say but cannot say it.”

Do the history, physical examination, and mental status testing support a diagnosis of primary progressive aphasia (PPA)?

■ WHAT IS PPA?

PPA is clinically defined as a progressive language deficit that leads to the dissolution of

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TABLE 1

Cognitive domains affected by PPA, Alzheimer disease, and vascular dementia

	LANGUAGE EXPRESSION	MEMORY REGISTRATION	MEMORY RECOGNITION	EXECUTIVE FUNCTION
Primary progressive aphasia	Very impaired	No change	No change	No change
Alzheimer disease	Impaired	Impaired	Very impaired	Impaired
Vascular dementia	Impaired	Impaired	Impaired	Very impaired

almost all language functions, while other cognitive functions remain relatively preserved until late in the course of the disease.

Although controversy exists regarding the nomenclature of PPA, several subtypes have been recognized. PPA can be either fluent or nonfluent, and with or without repetition or impairments in comprehension, reading, or writing.¹ PPA in which speech is nonfluent and agrammatical is known as *progressive non-fluent aphasia*. PPA with fluent speech but poor comprehension is called *semantic dementia*. PPA with fluent aphasia is also called *logopenic progressive aphasia*.

Depending on the type of aphasia, specific areas of the brain are affected.² Progressive nonfluent aphasia is associated predominantly with atrophy of both frontal lobes. Difficulty in naming and understanding words is associated with involvement of the left parietotemporal lobe. Difficulty with recognizing faces and objects is associated with involvement of the right temporal lobe.

Errors in speech may be semantic (word choice) or phonemic (sound-based). Speech may also be described as telegraphic (using abnormally short phrases). Examples of semantic errors in the sentence “I will come my house in your car and drive my car into Chicago” include the inappropriate use of “my” and “into Chicago” instead of “to Chicago.”³ The sentence “For exercise I like to runt and lit wastes” demonstrates phonemic errors in the substitution of “runt” for “run” and “lit wastes” for “lift weights.” Many of these errors can be identified during the patient interview.

Although PPA can appear in people as young as 35, the mean age of onset is in the

6th decade, and it arises only rarely after age 75. Patients experience isolated language problems for a median of 4.5 years (range 1–15) before seeking medical attention.⁴

PPA is primarily a sporadic disorder, but it can be inherited in an autosomal-dominant manner. Familial PPA has been described, and the disease has been linked to chromosomal locus 17q21.⁴ Early studies of apolipoprotein E genotyping in PPA do not indicate a predisposition with the E4 allele, which has been observed in Alzheimer disease.⁵

Neuropathologic studies demonstrate changes consistent with Alzheimer disease in 30% of PPA cases. In about 70%, the microscopic findings include focal spongiform changes and focal neuronal degeneration, resembling the neuropathological findings found in frontal lobe dementia of the non-Alzheimer type. An additional 20% of patients with PPA have Pick disease, characterized by tau-positive spherical neuronal inclusions.³

■ PPA VS STROKE, MASS LESION, ALZHEIMER DISEASE

The differential diagnosis of PPA includes stroke, mass lesion, and Alzheimer disease.

Dominant hemispheric stroke involving the language centers produces aphasia similar to the language deficits in PPA, but presents acutely, making confusion with PPA unlikely.

A slow-growing mass in the language center could also produce aphasia, but an imaging study would exclude this possibility.

Aphasia is common in Alzheimer disease but is almost invariably associated with early memory loss or other cognitive impairment.

**She states
'I know what I
want to say
but I can't
say it'**

Vascular dementia may have language problems associated with it, but cognitive deficits involving memory and executive function are more pronounced. **TABLE 1** shows areas of cognition characteristically affected by PPA, Alzheimer disease, and vascular dementia.

■ DIAGNOSIS IS CLINICAL

The diagnosis of PPA is based primarily on the history and physical examination. Laboratory testing is uninformative. Electroencephalography can demonstrate left-hemisphere slowing or, less commonly, diffuse abnormalities, but findings are normal in 75% of cases.

Computed tomography (CT) or magnetic resonance imaging (MRI) can show left temporal lobe atrophy, but these imaging studies are normal in 50% of cases. Functional neuroimaging with positron emission tomography and single-photon emission computed tomography (SPECT) can demonstrate left temporal hypometabolism. A recent study indicates that perfusion deficits demonstrated by SPECT precede morphological abnormalities identified by MRI or CT.⁶

Neuropsychiatric testing is useful to help differentiate the cognitive deficits of various dementing diseases. This battery of testing is more sensitive and specific for identifying cognitive deficits than the MMSE. It is also more precise in identifying what realms of cognition are decreased in function,⁷ especially language deficits, in which the MMSE is particularly weak. Prior to referral for neuropsychiatric evaluation, preliminary assessment of language can be done in the office. An example would be to ask the patient to identify geometric shapes, parts of the body, or components of common objects.³

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■ NO CURE, BUT SPEECH THERAPY CAN HELP

PPA is a degenerative disorder, and patients eventually develop severe dementia. Language impairment and functional communication can be positively and significantly influenced by speech therapy, regardless of whether the aphasia is chronic or acute and independent of the diagnostic type of aphasia or severity of deficit at start of care.^{8,9}

■ CASE REVISITED: DIAGNOSTIC WORKUP, TREATMENT, AND FOLLOW-UP

At the initial evaluation we thought the diagnosis of PPA to be likely. We obtained a thyroid-stimulating hormone level, complete blood cell count, basic metabolic panel, and vitamin B₁₂ level to rule out potentially reversible causes of cognitive impairment. Depression was suspected, and a trial of citalopram (Celexa) was started.

MRI of the brain demonstrated periventricular and subcortical leukoencephalopathy also involving the pons and mild global atrophy, changes that are not unusual for the patient's age. Electroencephalography was normal without focal or epileptiform activity. Neuropsychiatric testing evaluation supported a diagnosis of PPA.

Her mood improved with citalopram therapy. She was referred to a speech therapist, and she had objective improvement after 16 visits. At a later follow-up appointment, her family noted a further decline in speech but no other cognitive decline. The family was instructed to monitor her mood, and the patient was scheduled to undergo repeated neuropsychiatric testing.

Neuropsychiatric testing helps differentiate various dementing diseases

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