CASE REPORT

Primary progressive aphasia beginning with a psychiatric disorder

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INTRODUCTION

Primary progressive aphasia (PPA), frontotemporal dementia (FTD), and semantic dementia (SD) are clinical subtypes of frontotemporal lobar degeneration (FTLD). PPA is characterized by marked changes in language ability.[1] Although anxiety is identified in 39% of FTLD subjects, agitation, irritability, and depression may also be observed.[2] Frustration and anxiety have been frequently reported as early symptoms of PPA, but they are commonly construed by patients and their relatives as secondary consequences of the social embarrassment caused by the difficulty with language.[3] Similarly, the avoidance of social situations by these patients is frequently interpreted as a reaction to the loss of language abilities.

Here, we report a patient with PPA who initially presented with panic attacks. To the best of our knowledge, this is the first case of PPA manifesting with panic attacks as the first symptom. This case provides further evidence of the variable and circumscribed nature of the clinical presentation of focal cerebral degeneration.

CASE REPORT

A 75-year-old, right-handed widowed woman with 2 years of formal education first experienced a panic attack four years ago at the age of 71. She had no previous history of psychiatric disease or panic disorder. The panic attack was characterized by a sudden onset of symptoms, including palpitations, trembling, a sensation of shortness of breath, and a feeling of choking, which reached a peak within 10 minutes. During the subsequent months, the patient suffered from recurrent and unexpected panic attacks several times a week in crowded places and became afraid of feeling bad again in such places, soon developing agoraphobia. She was therefore given a diagnosis of panic disorder with agoraphobia. During the next few months, her panic attacks reduced in frequency after being prescribed sertraline at a dose of 50 mg/d.

Three years ago, the patient gradually started showing progressive isolated loss of language function (without significant impairment in other cognitive domains) characterized by a decline in linguistic fluency, word-finding difficulties, effortful speech, hesitant utterances with frequent pauses, phonemic paraphasias, and transpositional errors (e.g., 'animal' pronounced as 'amimal'). Her insight was preserved. Two years ago, she began to show diminished interest in her daily activities. One year ago, the process of dementia became more evident, with a progressive loss of independence and an increasing need for help from caregivers.

A magnetic resonance imaging (MRI) showed focal left temporal lobe atrophy (Figure 1). Ethyl cysteinate dimer (ECD) brain single-photon emission computed tomography (SPECT) showed severe hypoperfusion in the left temporal and inferior frontal regions (Figure 2). Both MRI and SPECT showed frank asymmetrical finds, and the left hemisphere more affected than the right.

Neuropsychological assessment was conducted with difficulty because of the severe communication and behavioral disturbances presented by the patient. As the majority of the classical neuropsychological tests are based on language skills, we resorted to more ecologically designed tests to examine the patient's cognitive function. She showed striking deficits in language tests, executive functions, and visuospatial processing. In addition, the patient exhibited strongly impaired verbal fluency (she was only able to name one animal in one minute in a *verbal fluency task*) and severe anomia (the inability to name even very easy figures, such as a house, tree, and comb in the *Boston Naming Test*). Her attention was impaired in many domains (visuospatial inattention, inability to maintain focus, distractibility, and working memory), and she could not recite automated sequences (e.g., counting from one to ten). Language tests revealed that both comprehension and expression of language were similarly impaired. She seemed be unable to recognize the colors and geometrical shapes presented in the *Token Test* and could not read (alexia) or write (agraphia). The patient's speech output was normal; however, it was unintelligible, and she could not engage in a conversation. She did not recognize famous faces (e.g., Pelé, Roberto Carlos, and Lula). Her performance was impaired even in neuropsychological tests less dependent on language skills. She showed constructive apraxia (she could not reproduce simple geometric forms) and some aperceptive agnosia (the *Boston Naming Test*). Her final Mini-mental State Examination (MMSE) score was five (one point for the day of the week, two points for immediate memory, and two points for verbal command). Finally, the patient was unable to understand how to arrange numbers to form a clock.

The patient was submitted to a workup for the differential diagnosis of dementia and to search for organic causes of

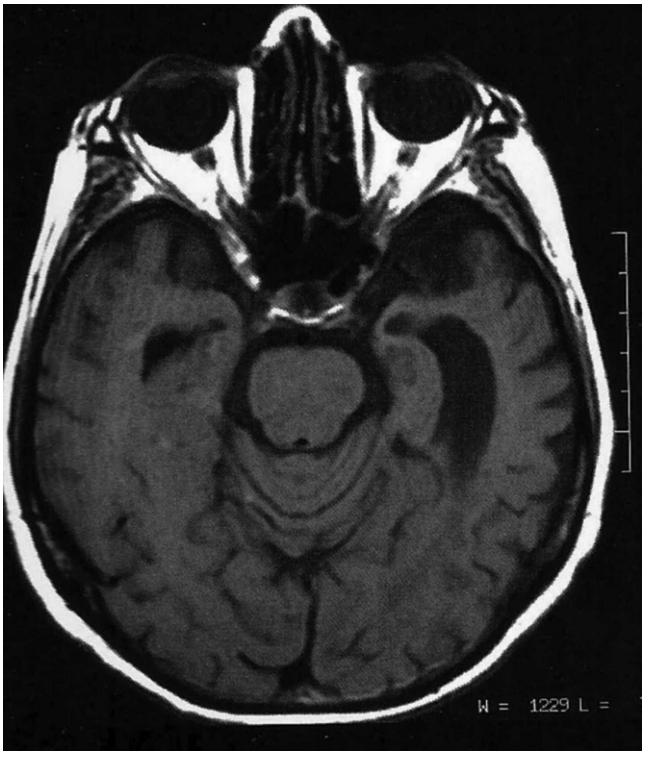

Figure 1 - MRI (axial T1) showing focal atrophy of the left temporal lobe.

anxiety. A complete blood count with differential; renal, liver, and thyroid function tests; determination of vitamin B12 and folic acid levels; syphilis serology; urinalysis; lipidogram; glycemic testing; hemosedimentation speed; and electrocardiogram and electroencephalogram were conducted. All of these test results were normal.

DISCUSSION

This case presented with panic attacks as a symptom of the initial phase of PPA. In this phase, the patient fulfilled the DSM-IV[4] diagnostic criteria for panic disorder with agoraphobia. Her language abilities gradually changed after the appearance of the panic attacks, with progressive anomia, loss of fluency, reduced verbal output, and inadequate use of generic words. Her previous medical and psychiatric histories were unremarkable, and she had no personal or familiar antecedents of panic disorder. It is rare to find a panic disorder (usually a disorder of young people) beginning in old age.[11] Moreover, the panic disorder presentation in this case was atypical, with fewer psychological symptoms (e.g., depersonalization, derealization, feeling of imminent death) when compared with classic (functional) panic disorder beginning at an earlier age. Thus, it is likely that the patient's first symptom of panic attacks at the age of 70 years was a symptom of early-stage dementia.

Traditionally, PPA is described primarily as a language deficit disorder. Conversely, FTD is essentially defined as a behavioral variant of FTLD. Our case demonstrates that these notions of PPA and FTD should not be viewed as rigid rules and that PPA can initially manifest with behavioral symptoms. In fact, PPA may be mistaken for a primary psychiatric disorder in many clinical situations[10]. Several neuropsychiatric symptoms such as depression, apathy and agitation have been reported in PPA.[5] Panic attacks have only been reported as a first symptom in one case of FTLD, but this case involved FTD and not PPA.[6] Therefore, this is the first report of PPA presenting with panic attacks and agoraphobia as the initial symptoms.

In our case, anxiety disorder cannot be described as a secondary consequence of the social embarrassment produced by language difficulties in PPA, as commonly assumed, as the panic attacks began before any language disorder was apparent. Similarly, the social withdrawal in this case cannot be explained as a psychological reaction to the social embarrassment produced by limited language skills; rather, it is better understood as an agoraphobic response to crowded environments.

The progressive language deterioration observed in this case, including the anomia, reduced spontaneous verbal output, loss of fluency, and phonemic paraphasic errors, is consistent with the clinical features of progressive aphasia as defined by Neary et al.[7] The findings of both focal atrophy of the left temporal lobe on MRI and left frontotemporal hypoperfusion on the ECD SPECT support the diagnosis of PPA. In contrast, episodic and semantic memory, perception, and spatial skills were all well preserved. Therefore, the patient was diagnosed with primary progressive aphasia.

A neuroanatomical hypothesis has suggested that panic disorder may result from the dysfunction of the ''fear network'' located in the center of the amygdala. A recent neuroimaging study[8] indicated that subjects with panic disorder have a smaller-volume amygdala compared with normal healthy subjects. Even in the early stages of FTLD,

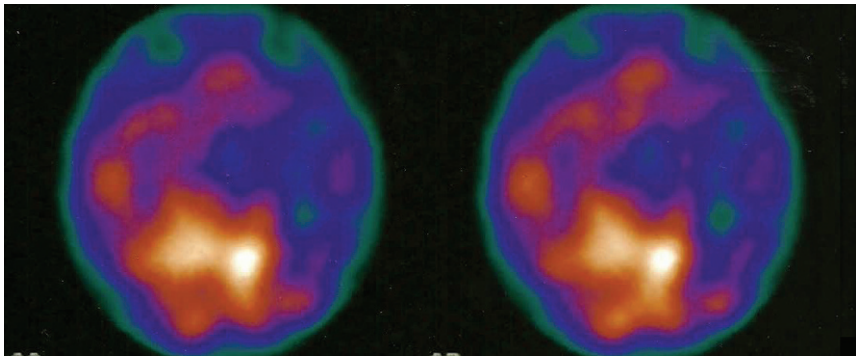

Figure 2 - SPECT (sequence of axial slices) showing left frontotemporal focal hypoperfusion.

atrophy of both the frontal lobe and the amygdala has been shown by quantitative structural neuroimaging.[9] In our case, the most affected brain area in the early phases of the disease was the temporal lobe, where the amygdala is located. Therefore, dysfunction of the amygdala might be associated with the panic attacks in this case. This finding may also be an important indicator of the precise neuroanatomical location where the neuropathological process of PPA begins.

In conclusion, we must carefully observe the course of elderly subjects diagnosed with panic disorder in old age because this psychiatric phenomenon may represent the beginning of a degenerative process involving dementia. Moreover, it is important to consider that PPA can manifest first with behavioral symptoms. Thus, behavioral symptoms should no longer be used as a characteristic that distinguishes between the early clinical indicators of PPA and FTD, as this class of symptoms is not exclusive to the latter. Further study may lend support to our assertion that PPA is inaugurated by psychiatric symptoms whose phenomenology is linked to the pathology of frontotemporal regions of the left hemisphere.

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