

Searching for words: primary progressive aphasia

Primary progressive aphasia is a more rare — or possibly underdiagnosed — condition often mistaken for frontotemporal dementia or Pick's disease. First symptoms often present as the inability to grasp the appropriate words in speech and as yet there is no known effective treatment. **Drs Demi Onalaja** and **Bushra Rauf** explore this rare form of dementia to help clinicians differentiate it from Alzheimer's disease and other causes of dementia.

Primarily progressive aphasia (PPA) is a rare form of dementia¹ characterised by the gradual dissolution of language with the preservation of other cognitive functions and activities of daily living until late in illness^{2,3,4,5}. It can also be defined as slowly progressive aphasia in the absence of accompanying signs of generalised dementia⁶. It has been found that, apart from language disturbances, the other cognitive domains are not impaired for at least the first two years of illness⁷. Global deficit may eventually supervene, but relentlessly progressive impairment of language remains in the forefront of the clinical picture¹. Memory, visual processing, personality and reasoning are well preserved until the advanced stages and help to differentiate it from Alzheimer's disease (AD) and frontotemporal dementia (FTD), including Pick's disease³.

Clinical presentation

As stated, primary progressive aphasia (PPA) is a disorder with prominent word finding difficulty but, in the early stages, comprehension of conversational speech remains intact⁸. It also called Mesulam Syndrome as Dr M Marsel Mesulam, director of Behavioural Neurology at Beth Israel Hospital in Boston (1982), presented the first detailed case study of PPA³.

Few families with hereditary PPA have been reported, but some families do show autosomal dominance. A chromosome mutation in tau exon 13

has been found in one family and a few have linkage to chromosome 17⁵. Onset occurs in patients between the age of 40–75 years, but appears most often in their 50s and 60s^{1,2}. Males with PPA outnumber females with ratio of 2:1 (66 per cent males; 34 per cent in female); 97 per cent are right-handed, three per cent left-handed.

A recent comprehensive review of the literature of 112 published cases revealed mean age at first medical contact was 64 years. Patients presented with complaints of word finding difficulties in 59 per cent, comprehension deficit in 32 per cent, naming deficit in 23 per cent as well as other complaints (speech hesitancy, phonemic paraphasias, dysarthria, slowed speech and stuttering)².

The language problem usually begins with word finding difficulties, which are more apparent to the patient than to others^{1,2,8}. Some patients remain at this stage for a prolonged period of time while others progress to steadily worsening dysphasia, this may be of fluent or non-fluent variety with variable comprehension deficit, though reading and writing are often relatively preserved.

Ultimately, the patient is likely to become mute and to lose all ability to communicate, at which time it is very difficult to assess the intactness of other cognitive functions. Dyspraxic difficulties may accompany the dysphasia but other cognitive deficits remain absent for a considerable time¹. Memory, at

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isolated only to left hemisphere while in 43 per cent of cases changes were bilateral. Changes involve perisylvian atrophy, widening of frontal horn mostly towards the left side but slowly progressive over time and becoming bilateral. Any evidence of infarction, haematoma or any space occupying lesion should be ruled out.

Electroencephalogram (EEG) shows asymmetrical slowing on the left. Positron emission tomography (PET) or single photon emission tomography (SPET) scan shows areas of reduced cerebral blood flow and low cerebral metabolism mostly in left frontotemporal lobe. Few patients show bilateral biparietal and bitemporal hypo metabolism typical of AD or the bifrontal hypo metabolism associated with other frontal lobe dementias^{1,2}. All treatable causes of dementia should be ruled out by doing routine blood investigations.

least in the non-verbal domain proves to be intact, along with reasoning, orientation and visuospatial functioning until after two years of illness^{1,3}.

Despite the severity of language deficit, most reported patients including severely affected are able to live at home. Daily living activities can be remarkably well preserved with patients continuing to care for themselves adequately, manage their house and finances — and even to drive until late in illness^{1,2}. Personality and behavioural changes occur in some patients in later stages of illness. Focal neurological signs occasionally appear such as right hemiparesis, right body posturing or right arm tremors.

Sometimes PPA is described as part of Pick's complex or clinical Pick's disease, which includes the clinically overlapping syndromes of frontotemporal dementia (FTD), primary progressive aphasia (PPA), cortico-basal degeneration (CBD), primary supranuclear palsy (PSP) or motor neuron disease (MND)^{9,10}.

The longitudinal course of PPA associated with clinical features and neuroimaging findings appear to be heterogeneous. Mesulam suggested that the disease is isolated to language disturbance for at least eight to 12 years with mean duration at this stage being 5.2 years^{1,2} before more generalised dementia is evident.

Investigation

Brain CT and MRI scan revealed abnormalities in 84 per cent of cases. In 56 per cent, changes were

Pathological findings

PPA is almost always associated with asymmetrical left hemisphere degeneration, but it was reported in one case⁹ that right hemisphere atrophy in a patient with PPA was associated with atypical right hemisphere dominance for language. This suggests that neuronal damage in PPA is tightly linked to underlying anatomy of language⁹. The primary auditory cortex (Heschl's gyri) in each temporal lobe transmits language signals to Wernicke's area in the dominant temporal lobe, which is involved in the comprehension of spoken language. From here the signals pass via the arcuate fasciculus to reach Broca's area, in the dominant frontal lobe, which governs the expression of speech. Neurones from Broca's area project to the motor area of the precentral gyrus. This is responsible for the control of speech musculature. Reports of underlying pathology are heterogeneous, mostly of neuronal loss with superficial spongiform degeneration but some patients show a picture overlapping with AD, Pick's disease (FTD), Creutzfeldt-Jakob disease and Lewy body dementia^{1,11}.

In the case study of 112 patients by Mesulam, underlying pathology was neuronal loss with spongiform degeneration in 38 per cent, neuronal loss without characteristic histological features in 25 per cent, AD in 19 per cent, Pick's disease in 13 per cent, Creutzfeldt-Jakob disease in six per cent, Lewy body pathology in one per cent¹².

Conclusion

While no available treatment is available

References

- Williams Alwyn Lishman Organic Psychiatry (third edition), Other disorders Affecting the Nervous System, Primary Progressive Aphasia: 752–753. The Blackwell Science publishers
- O'Brien J, Ames D, Burns A. Dementia (2nd edition). Hodder Arnold: 780–781
- Wicklund AH, Johnson N; Weintraub S. Preservation of reasoning in Primary progressive aphasia: Further differentiation from Alzheimer's disease and the Behavioural Presentation of Frontotemporal dementia. *Journal of Clinical & Experimental Neuropsychology* 2004; **26**(3): 347–55
- Doran M; Lamer AJ. Monozygotic Twins Discordant for Primary Progressive Aphasia. *Alzheimer's disease and associated disorders* 2004; **18**(1): 48–49
- Kreffth TA, Graff RN, Dickson DW, *et al.* Familial Primary Progressive aphasia. *Alzheimer's Disease & Associated Disorder* 2003; **17**(2): 106–12
- Maeck L, Meller J, Otto M, *et al.* A (beta) peptide (1–42), Tau protein and S-100B protein level in cerebrospinal fluid of three patients with primary progressive aphasia. *Neuroscience Letters* 2002; **333**(1): 33–36
- Joshi A, Roy EA, Black SE, Barbour K. Pattern of limb apraxia in primary progressive aphasia. *Brain & Cognition* 2003; **53**(2): 403–7
- Sonty SP, Mesulam MM, Thompson CK, *et al.* Primary Progressive Aphasia: PPA and the Language Network. *Annals of Neurology* 2003; **53**(1): 35–49
- Zhang YM, Wang YJ, Zhou Y, *et al.* Primary progressive aphasia: A case study. *Chinese Journal of Clinical Rehabilitation* 2005; **9**(5): 165–67
- Kertesz A. Pick Complex: An integrative approach to Frontotemporal Dementia – Primary Progressive Aphasia, Corticobasal Degeneration, and Progressive Supranuclear Palsy. *Neurologist* 2003; **9**(6): 311–17
- Rosen HJ, Karmar JH, Gorno Tempini ML, *et al.* Pattern of cerebral atrophy in primary progressive aphasia. *American Journal of Geriatric Psychiatry* 2002; **10**(1): 89–97
- Mesulam M, Weintraub S, Parrish T, Gitelman D. Primary progressive aphasia: Reverse asymmetry of atrophy and right hemisphere language dominance. *Neurology* 2005; **64**(3): 556–57

Key points

- Primary progressive aphasia (PPA) is a rare form of dementia.
- It is a disorder of word finding difficulties with intact comprehension of speech and activities of daily living and other cognitive impairments including memory until late in illness.
- Ultimately the patient is likely to become mute but is still able to function well independently.
- No evidence of any definite treatment in literature.

according to the literature, the diagnosis of PPA should be borne in mind by clinicians encountering patients with subjective loss of expressive language. It is all too easy to falsely reassure patients who do not show typical patterns of dementia.

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