Primary progressive aphasia as the initial manifestation of corticobasal degeneration. A “three in one” syndrome?

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Summary

In 1994, the term “Pick complex” was proposed to indicate significant clinical and pathological overlapping between primary progressive aphasia, frontal lobe dementia and corticobasal degeneration. We report the case of a 60-year-old man, who initially presented progressive non-fluent aphasia with orofacial apraxia, and subsequently, over a period of 3 years, developed mutism, pathological laughter, extrapyramidal rigidity, dystonia, alien hand syndrome and bulbar signs. An extensive haematological, immunological and biochemical work up was normal. The results of neuroimaging studies and neuropsychological tests, along with the clinical evolution, finally led us to the “three in one” diagnosis, supporting the concept of Pick complex.

KEY WORDS: corticobasal degeneration, frontotemporal dementia, progressive aphasia.

Introduction

Corticobasal degeneration has been widely described as a movement disorder, however, cognitive impairment is also increasingly noted along with more typical clinical manifestations of primary progressive aphasia as an initial sign.

Case report

In June 2000, a 60-year-old male shepherd, residing in an isolated mountain area, 60 km from the nearest village, presented with complete loss of speech output (mutism). As witnessed by his wife, who accompanied him to our hospital, he had started showing poor verbal fluency almost two years earlier. At that time, he developed difficulties finding words, which progressed to difficulties pronouncing selected words. Over the next year he further deteriorated to the point that even his wife was unable to understand him. His wife also recalled that initially, he had had difficulty whistling his sheep and blowing out matches, and that later he had started holding his mouth open for much of the time. Despite these problems, he maintained his active daily rural schedule. His medical and family history were negative and he had never consulted a physician. Notably, he had never received any kind of education and had spent his whole life in the mountains. General physical examination was unremarkable, his blood pressure was 130/70 mmHg and ECG was normal. Neurological examination revealed positive, easily elicitable, bilateral grasp, palmo mental, jaw jerk, glabellar and snout reflexes, as well as severe apraxia of the mouth, lips, cheeks, tongue and throat. However, swallowing was unimpaired and cranial nerve function was normal. He also presented mild cogwheel rigidity of both wrists, whereas his gait and the rest of his neurological examination (pyramidal, sensory, cerebellar) were normal. Voluntary and spontaneous speech were equally and severely affected, with the patient showing apparent mutism. Nevertheless, considering his non-existent education, his understanding of speech and comprehension remained relatively well preserved. In the first neuropsychological assessment (June 2000), he achieved a performance IQ of 82 on the Wechsler Adult Intelligence Scale (WAIS) (1) (lower cut-off score 79), whereas the verbal IQ could not be assessed at all, due to his mutism. On the Token test (TT)-short version (2), he scored 21/36, (lower cut-off score 29), on the Dot Center test (DCT) (3), he scored 20/20 (cut-off score 15), and Grade III on the Raven’s Progressive Matrices (RPM) (4) (cut-off II). He showed mild frontal impairment, scoring 7/15 (lower cut-off score 8) on the Weigl’s Sorting Task (WST), modified version (5). He was liable, at any time, to burst out laughing, in spite of the absence of external emotional stimuli, thereby demonstrating poor emotional output. He scored 27 (cut-off score 27) on the Frontal Behavioral Inventory (FBI) (6).

An extensive haematological, immunological and biochemical work up was normal, including thyroid function tests, serum vitamin B12, copper, ceruloplasmin, and homocysteine; specific serologic tests for HIV, syphilis, brucella, fungal and typhus infections were unrevealing. In addition, EEG, EMG, nerve conduction velocities, Tensilon test, mediastinal CT scan, extracranial-transcranial Doppler and cerebrospinal fluid cytchemistry and protein electrophoresis gave normal findings. Finally, brain
MRI revealed only mild left perisylvian atrophy (Fig. 1a). The patient was discharged, with a diagnosis of mutism-extrapyramidal syndrome of uncertain aetiology and received L-Dopa treatment (500 mg/day). Neurological examination one year later also revealed right hand dystonic posture, precipitated by action, right alien hand syndrome, left hemifacial spasm and difficulty swallowing. Pyramidal signs were evident in all four limbs and the cogwheel rigidity, unresponsive to the L-Dopa treatment, had increased in both upper limbs. His severely apraxic gait with tendency to fall forward led his becoming practically bedbound and unable to work or take care of himself. Neuropsychological test performances had also deteriorated. Performance IQ on the WAIS was 70, on the TT he scored 15/36, and on the DCT 18/20, his RPM grade was IV, and he scored 5/15 on the WST and 29 on the FBI. Follow-up brain MRI revealed marked left perisylvian atrophy (Fig. 1b).

The patient was lost to follow up. Through telephone contact with his wife we learned that he remained completely bedridden and was fed with great difficulty. His wife refused any further medical assistance.

Discussion
In 1994, the term “Pick complex” was proposed to indicate a significant clinical and pathological overlapping between primary progressive aphasia, frontal lobe dementia and corticobasal degeneration (CBD). Although recently supported by considerable clinical and pathological data (8-10), this concept has not been universally accepted (11). Kertesz et al. (9), described the clinical, neuropsychological and neuroimaging findings of 35 patients with CBD, along with autopsy results in 11 cases. To study longitudinally the relationship between the motor, language, cognitive and behavioural symptoms of CBD, the authors presented their combined prospective and retrospective experience of the syndrome and provided evidence for a relationship with the neuroimaging and pathological findings (9).

The case presented here is limited by a lack of neuropathology results. Nevertheless, the phenotype of this patient, along with the neuropsychological and neuroimaging deterioration over 3 years, support the concept of Pick complex (7,9), as well as underlining the importance of clinical follow up in similar “degenerative” disorders (11,12). One could question the validity of neuropsychological tests in an illiterate patient, such as the one we describe. However, although the relationship between dementia and cultural level is complex, the diagnosing of cognitive impairment in uneducated persons is not currently thought to constitute a problem (13).

Our case initially presented progressive non-fluent aphasia with orofacial apraxia and subsequently developed mutism, pathological laughter, extrapyramidal rigidity and dystonia, alien hand syndrome, and bulbar signs (9,12). Although it is difficult to define a disease on the basis of a series of symptoms or signs (14), this evolution, with evident clinical overlapping between the three nosologies of Pick complex (7,9,10), led us to the “three in one” diagnosis.

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Figure 1 - In June 2000 (a), axial brain MRI with enhancement revealed mild left perisylvian atrophy on T1 weighted images (TR 490 ms, TE 20 ms). One year later (b) marked left perisylvian atrophy was noted (TR 600 ms, TE 20 ms).
Primary progressive aphasia