Clinical approach to probable mixed vascular dementia and progressive supranuclear palsy

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Abstract

Probable-mixed dementia, combining vascular dementia and progressive supranuclear palsy (PSP), presents diagnostic challenges due to overlapping clinical features and radiological findings. This case report highlights the complexities involved in diagnosing such cases, where clinical manifestations evolve, requiring careful evaluation and periodic reassessment. Imaging plays a crucial role, with characteristic features aiding in distinguishing between different etiologies. Management of mixed dementia poses therapeutic dilemmas, particularly given the lack of effective treatments for PSP. Nonetheless, a comprehensive approach involving education, vascular risk factor control, and family support is essential for optimizing long-term patient and caregiver outcomes. This case underscores the importance of a multidisciplinary clinical and radiological approach in navigating the complexities of mixed dementia cases.

Introduction

Dementia persists as a global challenge, being a degenerative ailment. About 5.4% of individuals aged over 65 contend with dementia, its prevalence escalating with advancing age. Despite this, early diagnosis, management, and social support yield substantial benefits. However, diagnosing dementia poses challenges due to the myriad potential causes, and symptoms may progressively emerge, necessitating time for diagnosis. Additionally, dementia can stem from other ailments, resulting in cases of mixed dementia.[1,2]

Dementia, a complex and multifaceted neurodegenerative condition, presents a formidable challenge in clinical practice, particularly when its etiology involves a combination of factors. In this case report, we delve into a compelling instance of probable mixed dementia, featuring a confluence of vascular dementia and Progressive Supranuclear Palsy (PSP). Through meticulous clinical and radiological examination, we navigate the diagnostic journey of a patient initially diagnosed with vascular dementia, only to unravel the complexities of their condition as additional symptoms, such as upper gaze palsy characteristic of PSP, emerge over time. Consequently, the diagnosis of probably mixed dementia (vascular and PSP) was later established.

Through this case report, the author endeavors to enrich understanding and insight into dementia diagnosis, particularly for cases presenting with supplementary symptoms that may aid neurologists in arriving at a diagnosis aligned with the underlying pathology. Such insights profoundly impact patient management and prognosis in the future. This case underscores the intricate interplay between clinical presentation and radiological findings in diagnosing and managing mixed dementias, offering valuable insights for neurologists and clinicians grappling with similar diagnostic dilemmas.

Case Illustration

An 80-year-old male patient came to the neurology outpatient clinic at Cipto Mangunkusumo Hospital for a comprehensive cognitive function assessment with a referral diagnosis of Parkinson's disease dementia with a differential diagnosis of vascular dementia.

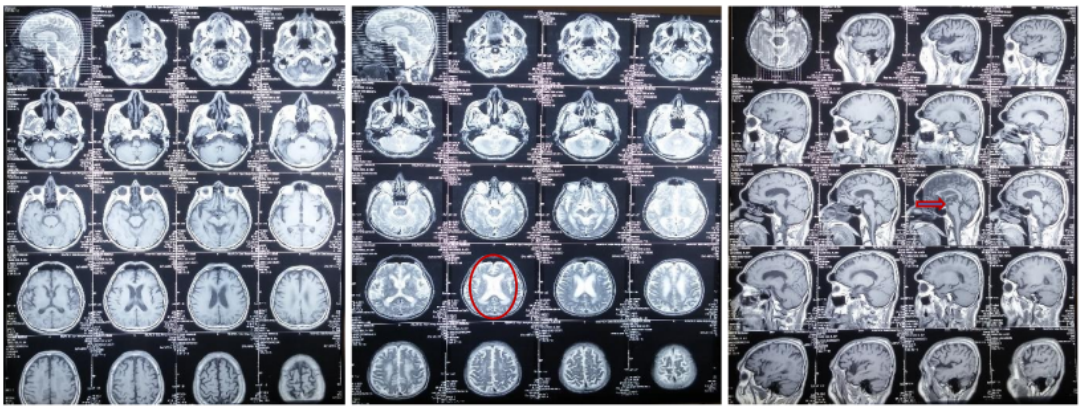
About a year ago, according to family members, the patient began experiencing frequent forgetfulness. The patient's son, who lives with him, is unsure exactly when these symptoms started, but he noticed that the patient's other symptoms were worsening day by day, and the forgetfulness was said to be worsening as well. Initially, the patient would forget things that were recently done or misplace objects but could still remember his children and family. The patient could also recall his home address and his orientation to time and place was still intact. Over time, the patient started forgetting the prayers and often repeated conversations and questions even though they had been answered previously. The patient sought medical attention, where a head MRI revealed signs of blockage in the brain. The patient was also noted to walk quickly and seemed to have difficulty stopping. The patient also complained of hallucinations, such as seeing things and sometimes hearing someone calling out. The patient then visited a psychiatrist and was prescribed risperidone 2x0.5mg.

Six months later, the patient experienced increased falls, particularly when rising from a seated position, and a perceived slowing of speech, although communication with family remained possible. Movement was noted to be slower. From the doctor's evaluation, the patient revealed postural hypotension as a cause of falls when transitioning from sitting to standing. While still able to walk independently, the patient's difficulty stopping led to supervision and assistance during walking. Additionally, occasional choking while eating and drinking was observed, though daily activities could still be performed independently albeit with slower movements. Following consultation with a psychiatrist, it was suggested that swallowing difficulties might be due to risperidone, prompting consideration for a change in medication. Hallucinations were reported to occur rarely with noted improvement.

The patient has had a history of hypertension for the past 10 years and has been regularly treated. Stroke, kidney problems, heart disease, diabetes mellitus, and a history of trauma are denied. In the family medical history, there is no history of hypertension, diabetes mellitus, stroke, or heart disease. The patient is married and has 6 children. He has a bachelor's degree, is currently not employed (retired civil servant), and lives with 2 of his children.

From the physical examination, the patient exhibited vital signs within normal limits. Overall, no abnormalities were noted. On neurological examination, the patient had a flat facial expression, with a Glasgow Coma Scale (GCS) score of E4M6V5. The patient's pupils were round with a diameter of 3mm/3mm, and direct and consensual light reflexes were normal. No neck stiffness was observed. Cranial nerve examination revealed upper gaze palsy. Motor strength in various muscle groups of the arms and legs was within normal limits, with normal physiological reflexes and negative Babinski sign. Sensory and autonomic examinations were normal. No tremors were present either at rest or with intention, but bradykinesia and rigidity were noted in both arms. The Romberg test was normal, and there were no signs of postural instability with the pull test.

Figure 1 depicts the results of the patient's head MRI examination. The examination results revealed periventricular leukoencephalopathy, cerebral atrophy with deep white matter ischemia (Fazekas grade III), and the presence of the hummingbird sign.



a) b) c)

Fig 1. Non-contrast head MRI.a) Axial T1-weighted image (T1WI), b) Axial T2-weighted image (T2WI) showing white matter lesions in bilateral periventricular areas (circle). c) Sagittal T1-weighted image (T1WI) revealing "*Humming bird*" sign (arrow).

In addition, the patient underwent a comprehensive assessment of higher brain functions, including evaluation of neuropsychiatric symptoms, language function, memory function, executive function, visuospatial function, emotions, and cognitive function. The results revealed mild naming impairment, delayed auditory and visual memory impairment, and executive function impairment consistent with vascular cognitive impairment. Then, the patient was examined one year later. Based on neurological examination, neuropsychological assessment, and head MRI findings, there were indications of upper gaze palsy, parkinsonism (rigidity), psychomotor slowing, recent memory impairment with preserved recognition, and visuoconstructional impairment significantly affecting daily activities, consistent with probable mixed dementia (PSP and vascular dementia).

Discussion

An 80-year-old male patient presented at the neurology outpatient clinic of RSCM with a referral diagnosis of Parkinson's disease dementia or vascular dementia. Considering the cognitive decline and suspicion of dementia, a more specific assessment of affected cognitive functions is necessary for a definitive diagnosis. Delirium and consciousness disorders, possibly due to metabolic abnormalities or psychiatric disorders, should be ruled out. Additionally, Alzheimer's disease needs consideration due to the patient's age and the uncertain onset of memory decline. The patient also experienced gait disturbances, walking faster, and having difficulty stopping, along with hallucinatory symptoms, leading to psychiatric consultation and the initiation of risperidone 2x0.5mg.

To distinguish between vascular dementia and Alzheimer's disease, specific diagnostic criteria are essential. Vascular dementia diagnosis encompasses possible, probable, and definite. A possible

diagnosis indicates dementia with focal neurological symptoms but lacks brain imaging confirmation or cognitive function impairment with a gradual onset and varying disease progression, along with clinical evidence of cerebrovascular disease. Thus, imaging tests are crucial to validate the diagnosis. Probable vascular dementia presents with early gait disruption, instability leading to frequent falls, urinary irregularities, pseudobulbar palsy, and personality changes resembling subcortical region disorders.[3-5]

The prevalent utilization leans towards the diagnostic standards established by NINDS-AIREN, defining dementia as a condition manifesting within 3 months post-stroke, or the manifestation of cognitive symptoms that emerge abruptly, fluctuate, or evolve progressively.[6] Given the existing diagnostic criteria and interpretations, along with clinical manifestations and imaging results in the patient, the experienced vascular dementia is classified as probable.

In differentiating it from Alzheimer's disease itself, particularly considering the initiation of symptoms in this case, which remains uncertain, poses a challenge. Conventionally, in Alzheimer's, the initiation progresses gradually and steadily, whereas vascular dementia may fluctuate despite an ongoing progressive decline. Considering additional symptoms such as disturbances in gait, the diagnosis of Alzheimer's becomes intricate since other focal neurological symptoms are not identified in Alzheimer's. Furthermore, neuropsychiatric disruptions in Alzheimer's tend to incline toward depression, anxiety, and delusions. Despite reports of neuropsychiatric symptoms like hallucinations in the patient, establishing a diagnosis solely based on these symptoms proves challenging. In Alzheimer's, memory degradation assumes a more prominent role, whereas vascular dementia disrupts executive function with relatively preserved memory compared to Alzheimer's.[6,7] Given the comprehensive spectrum of symptoms exhibited by the patient and corroborative investigations, including MRI findings of CSVD and prolonged hypertension risk factors, the likelihood of vascular dementia is heightened.

The next challenge lies in determining whether this case involves a mixed dementia, combining vascular and Alzheimer's, or instead presents as Parkinson's disease with dementia. Evaluation is conducted using the Hachinski Ischemic Score (HIS), where a score of 5 or 6 implies the diagnosis, albeit with limited specificity. In this instance, the HIS yielded a score of 8, indicating a higher likelihood of vascular dementia. There remains ongoing debate regarding classification: if Alzheimer's is accompanied by cerebrovascular disease, it's termed vascular cognitive impairment, no dementia (VCIND), potentially suggesting mixed dementia. However, if only vascular risk factors are present without clinical signs of Alzheimer's, suspicion of mixed dementia is unwarranted. Presently, no established postmortem neuropathological criteria exist for mixed dementia.[7]

8

Diagnostic criteria in Parkinson's Disease Dementia (PDD), include advanced age, dominant Parkinsonian symptoms, male gender prevalence, neuropsychiatric symptoms, and mild cognitive impairment (MCI). Distinguishing from Alzheimer's relies on cognitive impairments, with an accuracy of 74.7%. PDD primarily affects attention, executive function, and visuospatial abilities, sparing memory and language functions.[8]

In the patient's follow-up cognitive assessment after one year, memory and recognition improved, while hallucinations diminished. However, verbal fluency, executive function, and visuospatial abilities worsened. Memory function fluctuated, raising suspicion of vascular dementia over Alzheimer's. Additionally, deteriorating language, executive, and visuospatial domains, along with upper gaze palsy findings, raised concerns about Progressive Supranuclear Palsy (PSP). A repeat MRI showed hummingbird and morning glory flower signs. In idiopathic Parkinson's, MSA, and CBD, brainstem atrophy is absent, making the presence of the hummingbird sign significant for considering PSP.[9]

Initially thought to be a cause of atypical Parkinsonism, PSP has recently been found to exhibit significant clinical variation, including behavioral, language, and movement-related symptoms. According to the MDS PSP criteria, definitive diagnosis is only achievable postmortem, with potential diagnoses categorized as suggestive, possible, and probable. In the patient's case, based on these criteria, there is a level 1 likelihood for symptoms such as upper gaze palsy (O1), frequent falls over the past 6 months (P1), and parkinsonism symptoms characterized by rigidity-bradykinesia without tremor, pending confirmation of levodopa resistance (possibility A2), along with language impairment (C1). Consequently, the patient's PSP diagnosis could be deemed probable, with potential subtypes including PSP-RS with a combination of (O1 + P1) or PSP-P with a combination of (O1 + A2). However, since the patient hasn't received levodopa, the resistance to it remains unknown, suggesting a possible PSP subtype PSP-speech/language disorder (PSP-SL) with a combination of (O1 + C1). Swallowing difficulties developed in the patient after several months of taking antipsychotics for hallucinations (Risperidone). Clinicians should anticipate extrapyramidal symptoms when prescribing antipsychotic medications, though dysphagia caused by these drugs is rarely considered, as illustrated in this case with risperidone use triggering dysphagia. Reported dysphagia induced by antipsychotic medications is reversible and improves after dose reduction or switching to alternative drugs.[9-11]

Considering the discourse provided, a plausible diagnosis emerges as a probable mixed dementia, stemming from diverse backgrounds including vascular and PSP. This conjecture gains strength from imaging observations exhibiting distinct features of both ailments. Pharmacological management for the patient presents difficulties, given the absence of effective treatments, particularly for PSP, up to the present time. Nevertheless, an approach centered on education, vascular risk factor regulation, and familial support in caregiving remains pivotal for enhancing the long-term quality of life for both the patient and the caregiver.[3]

Conclusion

Dementia is a neurodegenerative disease with a multitude of etiologies, often coexisting with other neurodegenerative conditions. Achieving a definitive diagnosis for dementia is challenging due to the necessity of postmortem neuropathology, leading to considerations of suggestive, possible, and probable diagnoses. Diagnosing dementia also requires time, as neurological clinical symptoms may emerge gradually, leading to changes in the initial diagnosis. Through regular evaluations and

cognitive function assessments, clinicians can assess the likelihood of emerging neurological symptoms more accurately, thus guiding appropriate management and prognosis.

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