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Neuroleptic Malignant Syndrome in an Elderly Patient With Normal Pressure Hydrocephalus Overlapping Corticobasal Degeneration

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Abstract

In this case report, neuroleptic malignant syndrome (NMS) in an elderly patient with normal pressure hydrocephalus overlapping corticobasal degeneration was reported. The case highlights the need for clinicians to be cautious when using dopaminergic medication in the elderly patients, since these agents have risks for NMS which is a life-threatening complication. Additionally, co-occurrence of primary and secondary parkinsonian dementia syndromes should be kept in mind to avoid additional complications in the elderly patients.

Keywords

neuroleptic malignant syndrome, elderly, normal pressure hydrocephalus, corticobasal degeneration, dementia

Introduction

Neuroleptic malignant syndrome (NMS) is a life-threatening complication of dopamine-receptor antagonists such as antipsychotic and antiemetic drugs and characterized by a distinctive clinical syndrome of mental status change, rigidity, fever, and dysautonomia.[1,2] Although NMS is a rare situation, viewing from a geriatric perspective, the reports related to the NMS underscore the need for specific attention to the elderly patients, a vulnerable population due to predisposing factors, such as comorbidities, polypharmacy, dehydration, malnutrition, exhaustion, and underlying electrolyte abnormalities.[3,4] Diagnostic testings for NMS should include tests to rule out meningitis, encephalitis, systemic infections, heat stroke, and other drug-induced dysautonomias and laboratory evaluation of common metabolic sequelae of NMS, especially elevated creatinine kinase (CPK). Initial management of the patients with NMS should include discontinuation of neuroleptics, close inpatient monitoring of clinical signs and laboratory values, and supportive care. Dantrolene, bromocriptine, or amantadine may be considered for patients with CPK elevations or hyperthermia upon presentation or those who do not respond to withdrawal of the neuroleptic agent with supportive care within the first day or two.[1]

Corticobasal degeneration (CBD), a rare neurodegenerative disorder, is classically characterized by a progressive asymmetric movement disorder, including various combinations of akinesia, rigidity, dystonia, focal myoclonus, ideomotor apraxia, and alien-limb phenomena. This relatively rare parkinsonian dementia syndrome can be presented primarily with motor symptoms similar to those seen in Parkinson's disease, progressive supranuclear palsy, or multiple system atrophy.[5]

Normal pressure hydrocephalus (NPH) is characterized by urinary incontinence, subcortical cognitive dysfunction, and gait and balance disturbance, with enlarged cerebral ventricles in the absence of another cause, and the most commonly presenting symptom is gait disturbance.[6] Therefore, it may be misdiagnosed as a degenerative parkinsonian dementia disorder in the early stages.[7] In addition, NPH can be combined with age-related neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.[6]

Since we emphasized the interactions between drugs and comorbidities in the elderly patients, we presented an elderly patient with NMS having NPH overlapping CBD.

Case

A 75-year-old female was admitted to our geriatric department due to fatigue, palpitation, restlessness, tremor, insomnia, urgency, incontinence, gait and balance disturbance, and clumsiness in left upper limb and falling. The family reported that she had had an increase in fatigue, palpitation, changes in mental status, falling and tremor in upper limbs over the last week, had cognitive impairments and speech alterations over the past 8 months, urgency, clumsiness, and rigidity in left upper limb, incontinence, parkinsonism, and

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Table 1. Clinical and Laboratory Features of the Patient.

Comprehensive Geriatric Assessment		Before CSF Trap	After CSF Trap
COST[9]		26	27
MNA		11	
BADL		74	
IADL		8	
POMA-Gait		9	12
POMA-Balance		8	13
Up&Go, second		27	22
Laboratory Assessment	First day	Third day	Sixth day
WBC, cell/mm^3	5200		4700
Hemoglobin, g/dL	12.2		12.8
ESR, mm/h	34		30
CPK, U/L	962	437	59
Myoglobin, ng/mL	217	41.9	30.9
LDH, U/L	314	225	212
AST, U/L	41	34	16
Vitamin D, ng/mL	7.0		
Vitamin B12, pg/mL	289		
Folic acid, ng/mL	6.3		
TSH, IU/mL	0.6		

Abbreviations: AST, aspartate aminotransferase; BADL, basic activity of daily living (0 [worst]-100 [best]); COST, Cognitive State Test (0 [worst]-30 [best]); CPK, creatinine kinase; Hb, hemoglobin; LDH, lactate dehydrogenase; IADL, instrumental activity of daily living (0 [worst]-17 [best]); MNA, Mini Nutritional Assessment (0 [worst]-14 [best]); POMA, Tinetti Performance Oriented Mobility Assessment, POMA-Gait (0 [worst]-12 [best]), POMA-Balance (0 [worst]-16 [best]); TSH, thyroid-stimulating hormone; WBC, white blood cell; ESR, erythrocyte sedimentation rate; CSF, cerebrospinal fluid.

gait and balance disturbance over the past 2 years. She had a medical history of carbidopa (100 mg/d), entacapone (25 mg/d), L-dopa (200 mg/d), domperidone (30 mg/d), paroxetine (10 mg/d), and β-histine (16 mg/d) for CBD, depressive disorder, and vertigo. However, amantadine (100 mg/d) therapy was stopped due to inefficacy about 5 days before admission.

On physical examination, she had temperature of 37.4°C, pulse of 126 beats/min, respiratory rate of 18 breaths/min, arterial blood pressure of 120/70 mm Hg, ideomotor apraxia, lead-pipe rigidity especially in the upper extremities, alien limb in left upper extremity, mild hyperreflexia, postural instability, and grasp reflex. The biochemistry showed increased CPK, myoglobin, and lactate dehydrogenase and decreased vitamin D (Table 1). Because following withdrawal of amantadine and exposure to domperidone, all these positive findings, including rigidity, mental status alteration, elevation of creatine kinase more than 4 times the upper limit of normal, urinary incontinence, tachycardia and negative findings for infectious, toxic, metabolic, or neurologic causes, were taken into account, NMS was diagnosed according to expert panel consensus NMS diagnostic criteria.[8]

Immediately, cardiorespiratory monitorization was provided, paroxetine and domperidone therapies were discontinued, intravenous fluid therapy was administered, and low-molecular-weight heparin was prescribed to prevent deep venous thrombosis. After the supportive therapy, she began to feel better and the fatigue, palpitation, falling, and tremor gradually disappeared. Since discontinuation of the domperidone and supportive therapy improved her symptoms related to NMS, dantrolene, bromocriptine, or amantadine was not needed for her.

At the end of the 6th day of hospitalization, CPK levels were normal, but incontinence, gait and balance disturbances, clumsiness, psychomotor slowing, and impairment of attention, verbal fluency, executive function, and rigidity in left upper limb were in progress. Furthermore, magnetic gait was significant. Since it was thought that CBD was insufficient to explain all these clinical findings, especially her incontinence, magnetic gait, and psychomotor slowing, she was evaluated clinically and radiologically because of suspected CBD + NPH.

The magnetic resonance imaging scan supported the CBD + NPH (Figures 1 and 2). The cerebrospinal fluid (CSF) tap test was performed, and CSF pressure was recorded as 11 cm H_2O. After the CSF tap test, she displayed significant improvements in gait and balance and incontinence (Table 1). Since she didn't accept shunt surgery, acetazolamide (250 mg/d) was started.

Later, no further clinical and biochemical signs of NMS were observed and she was subsequently discharged. Two weeks later, she was reevaluated in our outpatient clinic and improvements in her attention, verbal fluency, incontinence, and gait and balance continued. She underwent rehabilitation program due to alien limb and clumsiness.

Discussion

Here, an elderly patient was reported to have cognitive impairment and parkinsonism due to the CBD and NPH accompanied by NMS, a drug-related syndrome. The importance of monitoring and controlling the use of dopaminergic medications among the elderly patients was underscored, given the risk of NMS, especially within the context of comorbidities that pose greater risk of additional complications with this case.

The differential diagnosis of parkinsonian dementia syndrome covers a broad spectrum of disorders that are neurodegenerative diseases, of which CBD is a highly rare primary parkinsonian dementia syndrome. On the other hand, NPH is the most common secondary parkinsonian dementia syndrome in the elderly patients, and in the early stages, it may be misdiagnosed as a primary parkinsonian dementia syndrome with its classical triad.[7]

Because there is no cure yet for CBD, some dopaminergic medications such as levodopa and amantadine may be effective on symptomatic improvement of parkinsonism in CBD.[10] However, the fact that abrupt discontinuation of these dopaminergic medications might be associated with NMS[1,10] should be kept in mind.

Neuroleptic malignant syndrome is quite rare but a potentially fatal complication which is not only associated with abrupt discontinuation of dopaminergic medications but also associated with dopamine-receptor antagonist such as domperidone and antipsychotics[1,2] frequently used in the elderly population.[4] In this case, it was thought that both domperidone therapy and abrupt discontinuation of amantadine therapy gave rise to NMS. Therefore, the drugs with dopaminergic effect, such as amantadine and domperidone, should be checked

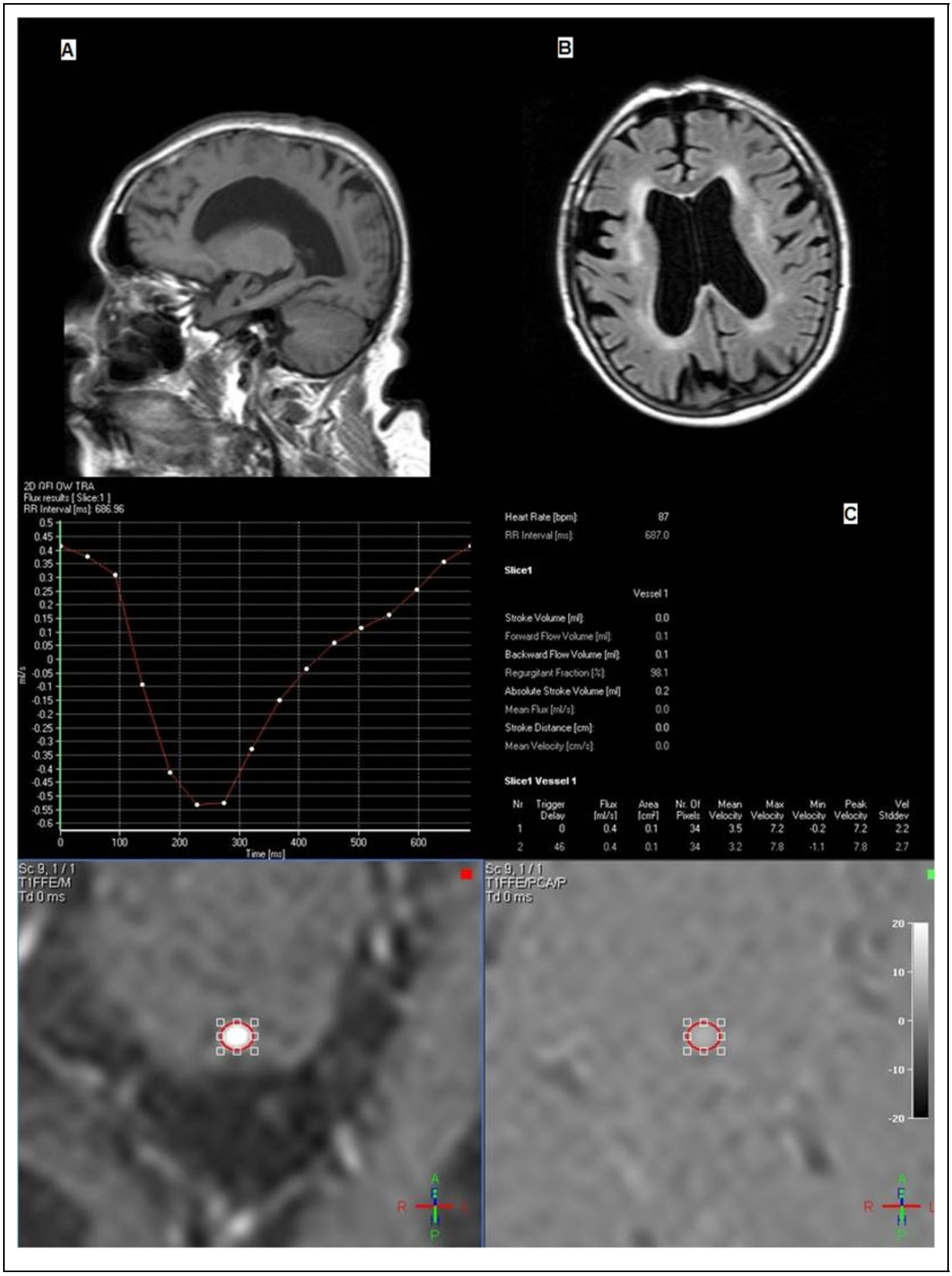

Figure 1. Brain magnetic resonance (MR) images of the patients. A, Parasagittal T1-weighted image. Enlarged lateral ventricle with increase in dorsal bowing of the callosal body due to hydrocephalus is obvious. B, Axial fluid attenuation inversion recovery (FLAIR) image at the level of the lateral ventricles. Note the disproportionately enlarged lateral ventricles compared with the relatively normal sulcal size. Bilateral perirolandic atrophy is also significant. C, Cerebrospinal fluid flow study with phase contrast MR imaging, the scout images (below), and velocity–time activity curve (above). Increased aqueduct stroke volume is calculated.

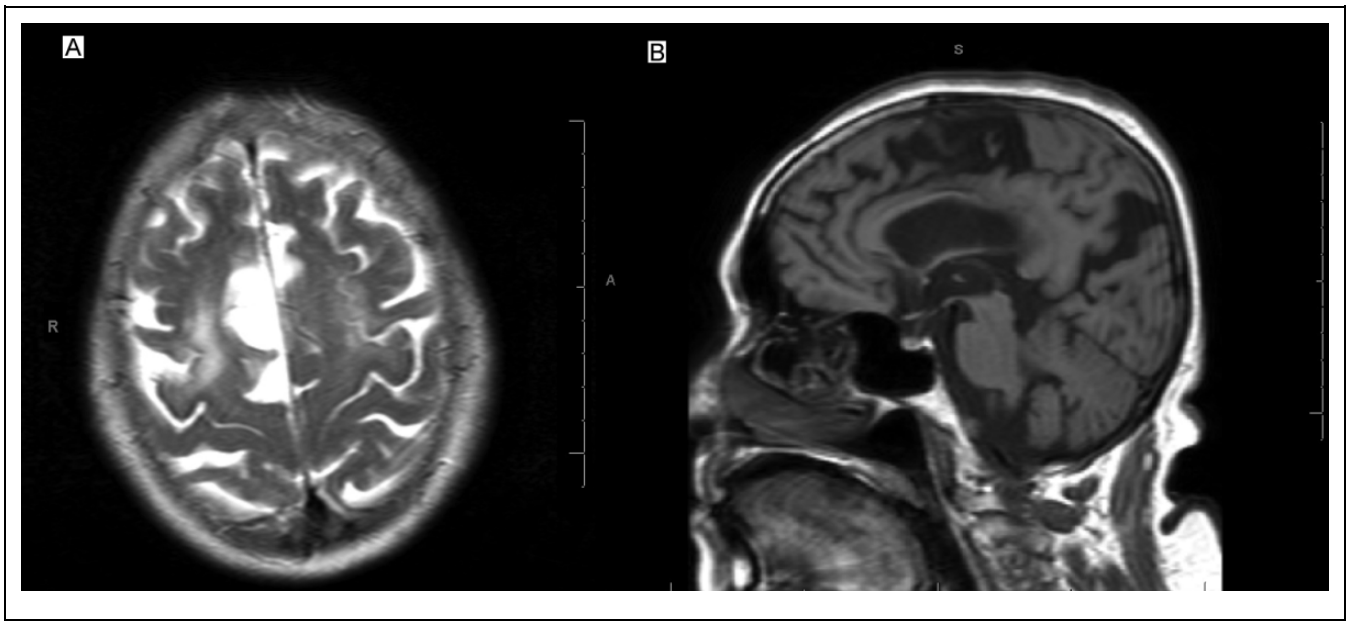

Figure 2. Asymmetrical cerebral atrophy in the magnetic resonance (MR) images. A, Axial T2-weighted image demonstrated asymmetrical cortical atrophy in right frontal convexity. B, Parasagittal T1-weighted image demonstrated enlarged lateral ventricle with asymmetrical atrophy in the parietal cortex and corpus callosum.

carefully in the elderly patients who are known to experience more adverse drug reaction. Of course NMS might not be unique in someone with an uncommon neurodegenerative syndrome, but for unexplained symptoms in an elderly patient with primary parkinsonian dementia syndromes such as CBD, additional parkinsonian syndrome such as NPH should be considered to avoid drug-related complications such as NMS.

In our case, after the clinical findings of NMS had been ameliorated, since we thought that CBD was insufficient to explain all these findings, both clinical and radiological findings were reevaluated due to a suspicion of NPH + CBD. Following the lumbar puncture, an improvement in her cognitive and motor abilities was demonstrated, so NPH overlapping CBD diagnosis was confirmed (Table 1). Thus, our patient with both primary and secondary parkinsonian dementia syndromes is one of the first cases reported in the literature.

Finally, it should be kept in mind that co-occurrence of primary and secondary parkinsonian dementia syndromes can be seen in elderly patients and that since dopaminergic medications are risky for NMS, such agents should be used carefully. Therefore, comprehensive geriatric assessment, including detailed neurological and radiological examinations, is recommended for the optimum management of elderly patients in order to avoid misdiagnosis and inappropriate treatment.

Declaration of Conflicting Interests

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