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Severe Normal Pressure Hydrocephalus Appearing in the Advanced Stage of Alzheimer's Disease: A Case Report

Morimatsu M[1]* and Kawai M[2]

[1]*Division of Neurology, Tokuyama Medical Association Hospital, Shunan, Japan*

[2]*Department of Neurology and Clinical Neuroscience, Yamaguchi University Graduate School of Medicine, Ube, Japan*

Abstract

The association of normal pressure hydrocephalus (NPH) with Alzheimer's disease (AD) is not uncommon. However, we herein report a rare case of AD that showed severe NPH at the late stage of AD. A 74-year-old woman developed forgetfulness without motor disturbances at 56 years old and was diagnosed with AD because of imaging findings showing atrophy of the fronto-temporo-parietal lobes on magnetic resonance imaging (MRI) and a decrease in the regional cerebral blood flow (rCBF) of the fronto-temporo-parietal lobes on single-photon emission computed tomography (SPECT). Eight years later, she showed progressive rigidity and akinesia of the arms and legs suggestive of parkinsonism, along with intermittent myoclonus of the arms, both more marked on the right. Her myoclonus was moderately controlled by oral clonazepam. She became bed-ridden at 74 years old and was admitted to our hospital (Tokuyama Medical Association Hospital) for endoscopic gastrostomy. At this time, head computed tomography showed severe NPH based on the radiological diagnostic criteria of idiopathic NPH (iNPH). We concluded no indication of ventriculoperitoneal shunt operation because of her severe dementia, and then she was transferred to a nursing home. This case is interesting, as the NPH imaging findings that appeared at the late stage of AD were striking. Her severe parkinsonism might have been due in part to NPH, although the myoclonus was considered to be of AD origin. Sequential radiological studies are useful for clarifying the clinical manifestations of AD patients.

Keywords: Alzheimer's Disease • Normal Pressure Hydrocephalus • Parkinsonism • Myoclonus

Introduction

AD patients associated with NPH have been well documented [1,2]. Some reports have found that the biopsy specimens of the brain in iNPH patients often showed AD pathology, suggesting that AD might induce NPH [3,4]. Progressive supranuclear palsy (PSP) and dementia with Lewy bodies (DLB), each associated with NPH, have also been reported [5,6]. Recently, Espay et al. [7] noted that ventriculomegaly mimicking iNPH was often a sign of neurodegeneration, terming this phenomenon neurogenerative NPH. This prompts questions of how iNPH and neurogenerative NPH differ and whether true iNPH exists [8].

In Japan, the diagnostic criteria of iNPH were established in 2012 by the Japanese Society of Normal Pressure Hydrocephalus [9] and have been widely used since then. The Japanese diagnostic criteria of iNPH include the three groups of "possible iNPH", "probable iNPH" and "definite iNPH". "Possible iNPH" includes all of the well-known clinical symptoms (gait disturbance, dementia and urinary incontinence) and MRI findings, characterized by narrowing of the sulci and subarachnoid spaces over the high convexity/midline surface, contrasting with enlarged lateral ventricles and subarachnoid spaces in other parts (disproportionately enlarged subarachnoid space hydrocephalus; DESH). DESH is crucial for discriminating iNPH from secondary ventriculomegaly derived from neurodegenerative diseases. "Possible iNPH" is appropriate when a cerebrospinal fluid (CSF) examination is not available, such as in a population-based cohort study. "Probable iNPH" requires normal CSF findings and an improvement in the symptoms after a CSF tap test. "Definite iNPH" requires an improvement in symptoms after shunt procedures.

The present case was an elderly woman with AD who showed severe NPH findings in the advanced stage of AD, which were entirely identical with those of "possible iNPH".

***Address for Correspondence:** Mitsunori Morimatsu, Head, Division of Neurology, Tokuyama Medical Association Hospital, Shunan, Japan, Tel: +81 834-31-2350; E-mail: m.morimatsu@tokuyamaishikai.com*

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Case Report

A 56-year-old woman without a remarkable family or personal history developed forgetfulness and difficulty writing Chinese characters. At 57 years old, she visited the neurologic clinic of Yamaguchi University Hospital. She was able to carry on a normal conversation and perform simple tasks in activities of daily living (ADL) without aberrant behaviors. A Wechsler adult intelligence scale-revised (WAIS-R) examination revealed a Verbal intelligence quotient (VIQ) of 98, a Performance intelligence quotient (PIQ) of 72, and a Total IQ of 86, suggesting mild dementia. She showed geographical disorientations and ideomotor apraxia. Her deep tendon reflexes were normal without positive plantar responses. Muscle tonus and co-ordinations were normal without gait disturbance.

Brain magnetic resonance imaging (MRI) showed diffuse cortical atrophy that was more marked on the right than on the left (Figure 1). 99mTc-l-hexamethyl-propyleneamine oxime (HMPAO) single-photon emission computed tomography (SPECT) showed a decrease in the regional cerebral blood flow in the bilateral fronto-parieto-temporal lobes, with findings more marked on the right than on the left (Figure 2). Her clinical features, including the brain images, were consistent with those of AD, so she was diagnosed with AD. Oral donepezil hydrochloride at 5 mg per day was given without any obvious effect.

At 64 years old, she showed rigidity of all the limbs, more prominent on the left than on the right, and a stooped posture with small steps and a shuffling gait, revealing parkinsonism. Furthermore, she developed occasional myoclonus of both arms that was not synchronous between the sides and was more marked on the left than on the right, without loss of consciousness. Follow-up brain computed tomography (CT) at this time showed increased brain atrophy without findings of iNPH. Her parkinsonism increased in severity thereafter without response to levodopa, while her myoclonus moderately decreased in frequency and intensity by oral clonazepam.

At 66-years-old, she was unable to walk and used a wheelchair every day. She spoke no meaningful sentences, often uttering such logoclonus as Ah-Ah-Ah-Ah. At 73 years old, she was admitted to Tokuyama Medical Association Hospital because of difficulty chewing and swallowing. Her speech was only logoclonus. She showed severe rigidity of all limbs, revealing contracted flexion postures at the elbows and knees. Intermittent myoclonus of a mild degree in both arms was seen. Laboratory data showed malnutrition (serum albumin 2.7 g/dl). Brain CT was performed instead of MRI because the latter seemed difficult to conduct due to the myoclonus of the arms. On brain CT, striking images of "possible iNPH" were noted, with remarkable ventriculomegaly associated with DESH according to the criteria of iNPH [9] (Figure 3). The oral intake of food was impossible, so percutaneous endoscopic gastrostomy (PEG) was performed.

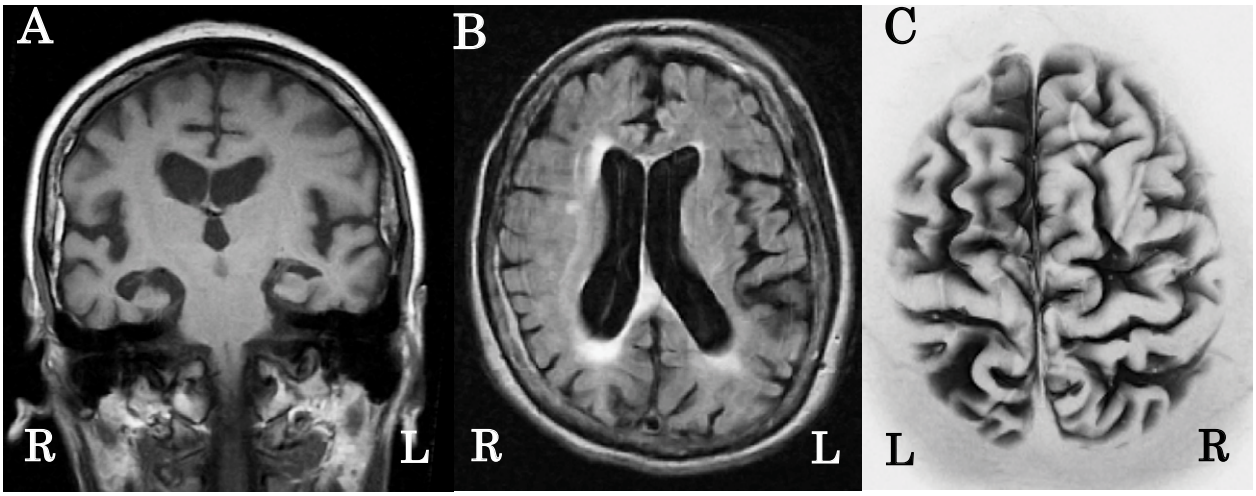

Figure 1. Head MRI at 57 years old revealed diffuse cortical atrophy, along with atrophy of the bilateral hippocampi and a mild degree of ventriculomegaly, more marked on the right than on the left. No findings of NPH were seen. (A) T1-weighted image, (B) fluid-attenuated inversion recovery (FLAIR) imaging and (C) surface anatomy scanning imaging

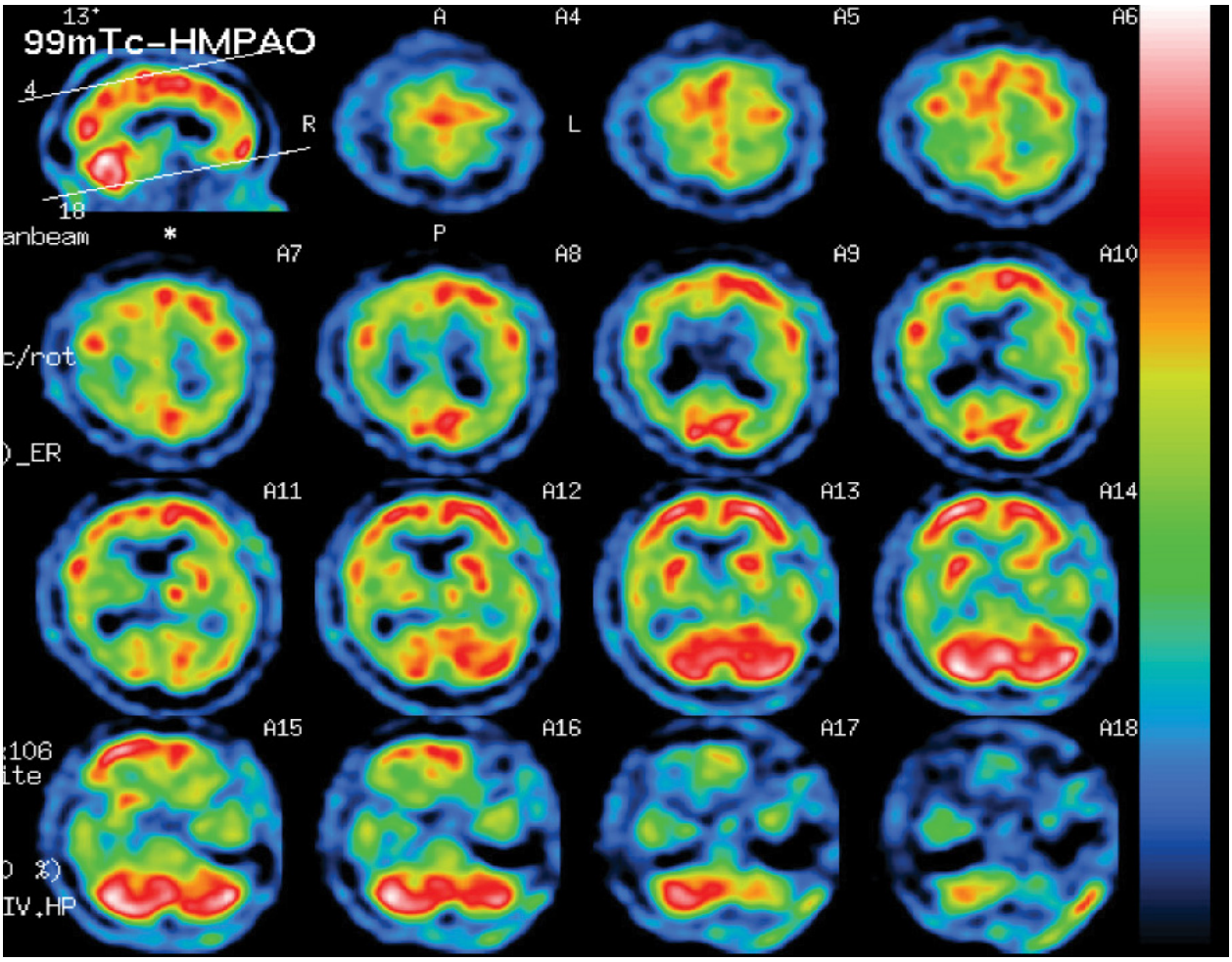

Figure 2. ^{99m}Tc-HMPAO SPECT at 57 years old showed a decrease in the regional cerebral blood flow in the bilateral fronto-parieto-temporal lobes, more marked on the right than on the left.

Thereafter, her clinical course was uneventful, with improved nutrition, and she was transferred to a nursing home six months after admission. At this time, intermittent myoclonus of the arms persisted, and she showed complete mutism.

Discussion

This case was interesting because, in the early half of the clinical course, she showed clinical symptoms and brain images consistent with typical AD. In the later half, she developed parkinsonism, intermittent myoclonus and brain images mimicking iNPH. While comorbidity of AD and NPH is well recognized, which precedes the other is unclear. However, most reports have described patients with clinical iNPH features present at the same time as AD pathology on a brain biopsy [3,4] or positive AD biomarker detection in CSF [2]. Recently, Kang et al. [10] reported a clinical case with extremely severe NPH imaging findings on MRI who also showed intellectual deficits consistent with AD and positive amyloid imaging on positron emission tomography (PET). Therefore, patients who exhibit the typical clinical course of AD followed by remarkable iNPH brain imaging findings in the advanced stage, as seen in our patient, seem to be uncommon.

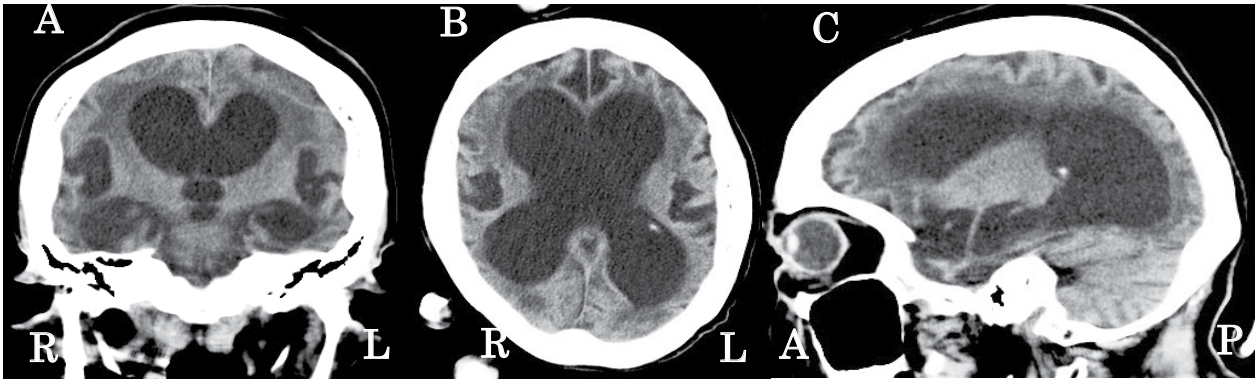

Figure 3. CT at 73 years old revealed extreme ventriculomegaly accompanied by DESH mimicking "possible iNPH". (A) Coronal, (B) Axial, and (C) Sagittal sections.

There is controversy regarding whether or not iNPH even exists, as some researchers argue that most cases of iNPH can be derived from underlying neurodegenerative disorders, thus explaining why shunt operation of the cerebrospinal fluid often loses efficacy within a few years [7]. We may thus question, "Does true iNPH actually exist?" [8].

Parkinsonism is frequently seen in iNPH [1] as well as in AD. It was previously mentioned that, in cases of rapidly progressive late-onset (beyond 65 years of age) AD, gait disturbance and rigidity are observed in 66% and 50% of patients, respectively [11]. With reference to the coexistence of Parkinson's disease (PD), Lewy body pathology indicating "Lewy body disease" (PD or DLB) was seen in 87 (25.1%) of 347 AD autopsy cases [12]. Although the PD in the present case might have coexisted with AD, severe NPH may have contributed to the development of progressive parkinsonism. Myoclonus in AD is not rare, with a reported prevalence of 8.5% among 1, 320 AD patients [13]. In another report, it was seen in 75% of the late-onset AD patients [11]. In these patients the origin of myoclonus was thought to be cortical. Non-synchronous myoclonus of bilateral arms without loss of consciousness may be rare, although the focus of origin was unexplored. Finally, controversy persists regarding whether ventriculoperitoneal or lomboperitoneal shunt is advisable or not in patients with neurodegenerative NPH. This is because the advantages associated with this operation, even in effective cases, tend to last only a few years [7]. For this reason, in our AD patient, shunt operation was not considered.

Conclusion

We concluded no indication of ventriculoperitoneal shunt operation because of her severe dementia, and then she was transferred to a nursing home. This case is interesting, as the NPH imaging findings that appeared at the late stage of AD were striking. Her severe parkinsonism might have been due in part to NPH, although the myoclonus was considered to be of AD origin. Sequential radiological studies are useful for clarifying the clinical manifestations of AD patients.

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