



# Does Vascular Dementia Exist? Report of Two Cases Previously Diagnosed with Vascular Dementia Treated by Means of Ventriculoatrial Shunts

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## Abstract

Vascular dementia (VaD) is the second most common cause of dementia after Alzheimer's disease. While new therapeutic modalities have been available for Alzheimer's disease, there is currently no effective treatment for VaD. We encountered two cases with VaD who recovered their cognitive function to normal levels after ventriculoatrial shunt (VA shunt). Both cases complained cognitive impairment shortly after cerebral infarctions. Their brain images showed ventricular dilatation without the findings of disproportionately enlarged subarachnoid space hydrocephalus, which is regarded as characteristic for idiopathic normal pressure hydrocephalus (iNPH). Both cases were initially diagnosed as VaD by board neurosurgeons. However, since they showed positive response to lumbar tap test, VA shunts were performed. Both cases recovered their cognitive function to normal level. Their excellent cognitive outcomes after VA shunts indicate that many iNPH patients with lacunar infarcts may possibly be misdiagnosed as VaD.

## Keywords

- ▶ dementia
- ▶ DESH
- ▶ iNPH
- ▶ VA shunt
- ▶ vascular dementia

## Introduction

Vascular dementia has been known for a long time.<sup>1,2</sup> In recent Japanese etiological study, VaD accounts for 18.9% of all dementia cases in the elderly population ( $\geq 65$  years old), making it the second most common cause of dementia after Alzheimer's disease (AD).<sup>3</sup> Based upon extensive research on AD,<sup>4–8</sup> the diagnostic accuracy has improved and new promising treatments have been developed.<sup>9–14</sup> However, it is still difficult to diagnose VaD correctly,<sup>15,16</sup> and there is currently no effective treatment for VaD beyond prevention of cerebrovascular diseases. We have experienced two cases previously diagnosed

as VaD by board neurosurgeons whose dementia were recovered to normal levels after ventriculoatrial shunts (VA shunt). In this brief report, we present their clinical courses and discuss the diagnostic challenges and treatment possibilities for VaD.

## Case Reports

### Case 1

A 71-year-old man presented with complaints of dementia, gait disturbance, urinary incontinence, and irritability. At the age of 69 he had collapsed with loss of consciousness and was hospitalized for 2 weeks with diagnosis of cerebral

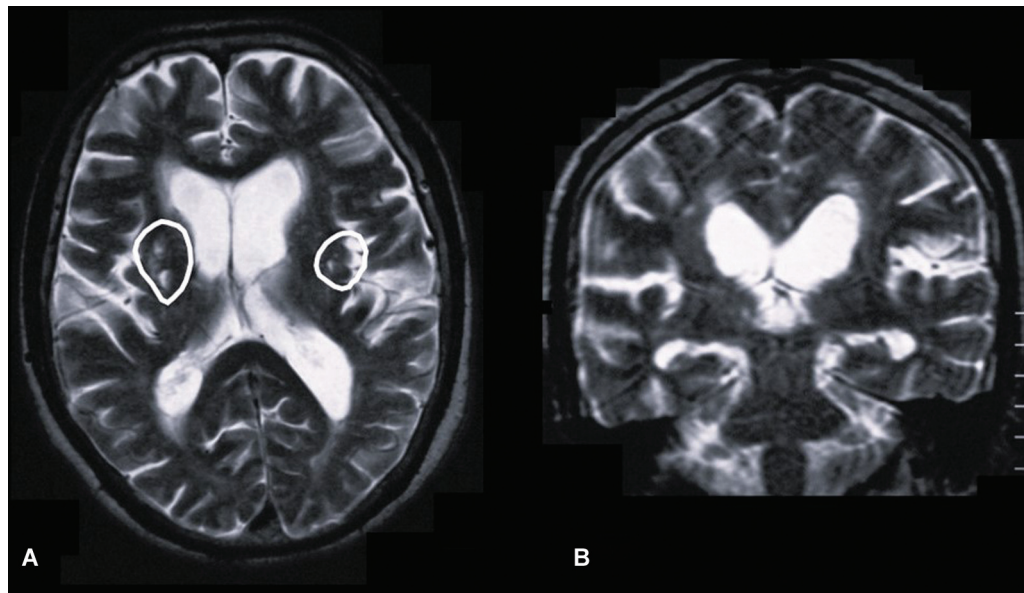
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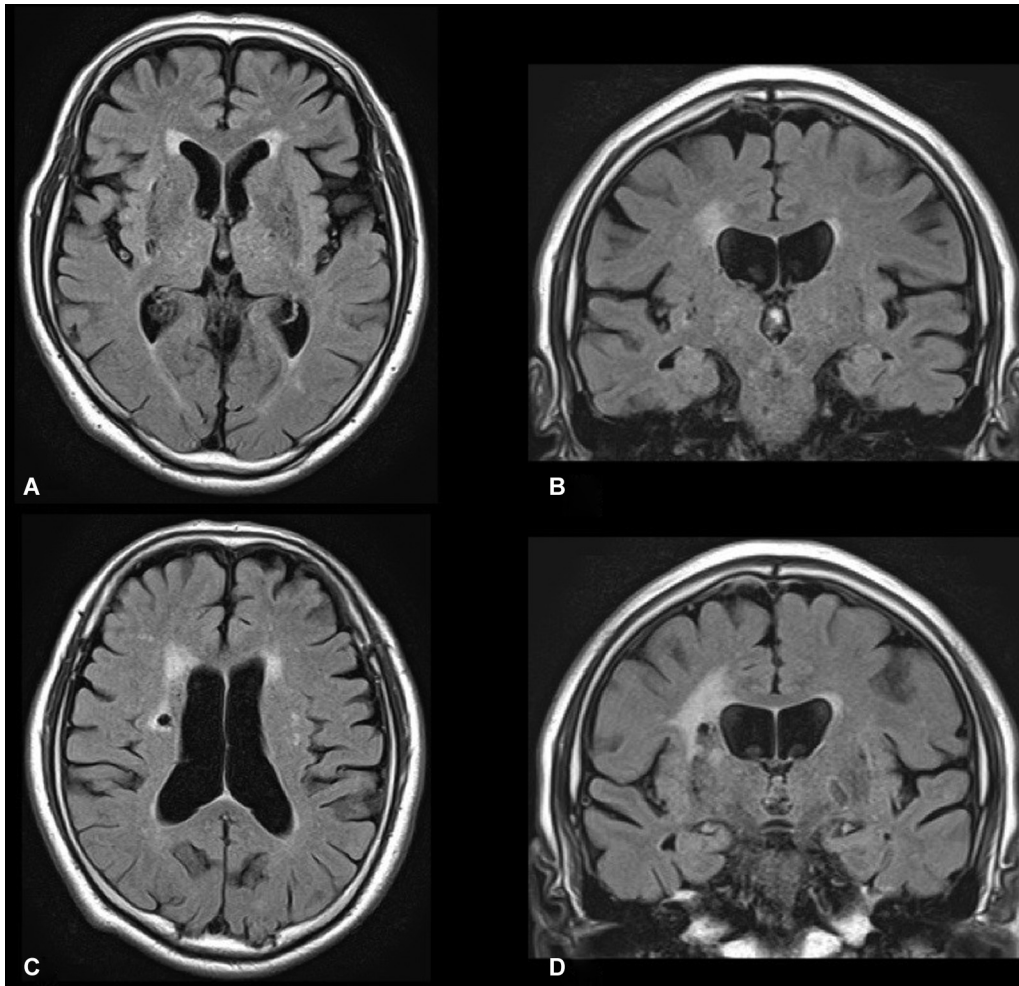
**Fig. 1** Multiple lacunar infarct in Case 1. (A) Evans' index is 0.34. Freehand circles were drawn by the board neurosurgeon to show lacunar infarcts. (B) Neither abnormal Sylvian fissure dilatation nor high convexity tightness were observed.

infarction. Although he was discharged without paralysis, his gait had become unstable after discharge. Because his memory worsened at the age of 70, he visited a board neurosurgeon. He was diagnosed as having VaD due to lacunar infarctions (**Fig. 1A**), and it was told to him and his wife that his dementia was untreatable. The symptoms continued to progress, and when he visited a nursing home at the age of 71, he had severe gait disturbance (mostly confined to a wheelchair), urinary incontinence, dementia, and irritability. Although the finding of disproportionately enlarged subarachnoid space hydrocephalus (DESH)<sup>17,18</sup> that is one of the image diagnostic criteria of idiopathic normal pressure hydrocephalus (iNPH)<sup>19</sup> was not observed on his magnetic resonance imaging (MRI) at the age of 70 (**Fig. 1B**), ventricular enlargement defined by Evans' index (EI)<sup>19,20</sup> was noted. EI was 0.34 (**Fig. 1A**). Though he was diagnosed with VaD for over 2 years because of multiple infarcts on MRI, we suspected he also had iNPH. His Japanese iNPH grading scale (J-iNPHGS)<sup>21</sup> was 11 points (gait disturbance: 4, cognitive impairment: 3, urinary dysfunction: 4), mini-mental state examination (MMSE)<sup>22,23</sup> was 10/30 and modified Rankin scale (mRS)<sup>24</sup> was 4. Lumbar tap test was performed to confirm the indication of VA shunt. The cerebrospinal fluid (CSF) pressure was 105 mm H<sub>2</sub>O and 50 mL of clear CSF was drained. After that the patient was able to stand up from wheelchair and walk. Although his MRI did not have the finding of DESH, he was diagnosed with probable iNPH<sup>19</sup> and a right VA shunt was performed. A pressure adjustable valve: Medtronic STRATA Valve Small, Pressure setting (performance level P/L = 1.5) with closed end atrial catheter with slits (Medtronic reduced tip) was used. The atrial catheter was inserted into the superior vena cava by puncturing internal jugular vein. The catheter was inserted approximately 5 cm from the puncture site. The operation time was 43 minutes. The patient did not come for regular follow-up evaluation and postoperative Timed Up and Go and MMSE

were not examined. However, semiquantitative evaluations were possible at 1 year postoperatively. J-iNPHGS was 2 points (gait disturbance: 1, cognitive impairment: 1, urinary dysfunction: 0) and mRS was 1. There were no apparent problems with memory, and the patient remembered going to watch sports and remembered the destinations of trips. Irritability disappeared completely and the patient's personality became calm just like before the onset on the cerebral ischemia. He was able to live independently at home with his wife. The patient died of heart failure 2 years and 5 months postoperatively.

## Case 2

A 69-year-old male presented with complaints of gait disturbance, dementia, urinary incontinence, emotional instability (easily moved to tears), and irritability. In the past at the age of 65, he was hospitalized for 2 months due to cerebral infarction (left hemiparesis). After discharge he developed urinary incontinence and gait disturbance. His cognitive function declined significantly. He no longer was able to write and gradually became unaware of his actions. He became emotionally unstable, was easily prone to tears, and very irritable. When he visited an outpatient clinic after discharge, he was diagnosed with VaD by a board neurosurgeon. Both him and his wife were informed that he did not need to consult anymore with regard to his dementia because he had untreatable VaD. His wife happened to see a TV program that described about iNPH. She noticed similarities between his symptoms and those of iNPH, so she took him to see one of the authors (KT). His MMSE score was 24/30, J-iNPHGS was 7 points (gait disturbance: 3, cognitive impairment: 2, urinary dysfunction: 2), and his mRS was 3. His MRI showed an EI of 0.27, with no DESH findings (**Fig. 2**), but it revealed abnormalities of ventricular shape such as third ventricular ballooning and anterior horn rounding, which were different from normal findings and atypical



**Fig. 2** Multiple lacunar infarcts in Case 2. (A) Evans' index is 0.27 and anterior horn roundedness was seen. (B) No abnormal Sylvian fissure dilatation or high convexity tightness were noted. Third ventricular ballooning was observed. (C) Lacunar infarct in the corona radiata is clearly seen. (D) No abnormal Sylvian fissure dilatation or high convexity tightness were noted. Third ventricular ballooning was observed. Multiple lacunar infarcts are seen.

neuroimaging findings of iNPH.<sup>23</sup> Based on these findings the possibility of iNPH was considered. Lumbar tap test was performed to confirm the indication of VA shunt. The CSF pressure was 120 mm H<sub>2</sub>O, and 50 mL CSF was drained. Shortly after the procedure, the patient reported significant improvement in gait (10-m walking time reduced from 23.2 to 8.8 seconds) and the clarity of speech also improved. Despite being an atypical case with accompanying lacunar infarction, he was diagnosed with probable iNPH<sup>19</sup> and right VA shunt was performed. The same VA shunt procedure as in case 1 was performed, except that a Codman Hakim programmable valve with siphon guard was used as the pressure adjustable valve. The operation time was 32 minutes. The initial valve pressure setting was 120 mm H<sub>2</sub>O based on the CSF pressure. At the regular 1-month follow-up, the J-iNPHGS improved to 2 points (gait disturbance: 1, cognitive impairment: 0, urinary dysfunction: 1). Because the computed tomography (CT) showed subdural hematoma due to over drainage, the pressure setting was increased to 200 mm H<sub>2</sub>O. Although symptoms worsened temporarily due to the increase of valve pressure, his subdural hematoma was treated conservatively. The valve pressure was gradually

lowered reaching 70 mm H<sub>2</sub>O 4 years after the surgery. The MMSE score improved to 28 at 1 year postoperatively, and the J-iNPHGS improved to 1 (gait disturbance: 1, cognitive impairment: 0, urinary dysfunction: 0). Even after 5 years 6 months the scores remained at 27 and 1, respectively. Although he had left hemiparesis due to lacunar infarction, he was able to walk without a cane and had no urinary incontinence, emotional incontinence, or irritability. He led an independent life, working in the fields for over 5 years and passed away from heart failure 5 years 8 months after the surgery.

## Discussion

### Summary of Cases

We report two cases previously diagnosed as VaD by board neurosurgeons without any treatment for over 2 years whose cognitive functions improved to normal levels shortly after the VA shunts. Both the patients were able to lead independent lives until their deaths. They both fulfilled the diagnostic criteria of VaD.<sup>25</sup> Although both cases exhibited the triad of iNPH, their imaging findings did not meet the diagnostic

criteria of the guidelines.<sup>19</sup> Instead, they were diagnosed with VaD due to lacunar infarction, which deprived them of the chances to receive lumbar tap tests for more than two years and consequently they did not receive CSF shunt surgeries.

### **Basis for Performing Ventriculoatrial Shunt in the Two Cases**

There are many causes of dementia.<sup>26,27</sup> INPH is one of the well-known causes of treatable dementia<sup>19,28–32</sup> that is characterized by the triad of gait disturbance, cognitive impairment, and urinary incontinence.<sup>19,31</sup> CSF shunt placement is currently only a reliable treatment.<sup>19,31</sup> Ventriculo-peritoneal (VP) shunt and VA shunt are most commonly used shunt configurations internationally;<sup>31</sup> lumboperitoneal (LP) shunt is commonly used in iNPH in Japan.<sup>33</sup> Although a meta-analysis disclosed that outcomes did not differ significantly among different CSF diversion techniques,<sup>34</sup> VA shunt patient were less likely to experience shunt obstruction and require shunt revision compared with VP-shunted patients.<sup>35</sup> Furthermore, total length of the shunt system (ventricular catheter + valve and flushing device + atrial catheter = 40 cm) is much shorter than that of VP and LP shunt systems and the pressure difference between the inlet (lateral ventricle) and the outlet (atrium or vena cava superior) of the VA shunt system does not change drastically by the change of body position (from recumbent to upright) that guarantee the constant CSF flow. Therefore, we had started to treat iNPH patients by means of VA shunts just before the first edition of Japanese guidelines was publicly available<sup>36</sup> (Japanese version was published in May, 2004). We have made it a rule to perform lumbar tap tests for those cases showing one or more symptoms of iNPH triad<sup>19,31</sup> and exhibiting imaging findings such as anterior horn rounding, third ventricular ballooning, Sylvian fissure dilatation, and convexity subarachnoid space enlargement.<sup>29</sup> If symptoms improve even temporarily, VA shunt is chosen as the first-line surgery, and favorable outcomes have been achieved.<sup>29,37,38</sup> Although the ventricular dilatation is a mandatory condition for the diagnosis of iNPH and the definition of the dilatation is  $EI > 0.3$ ,<sup>19,31</sup> this thresholding value was determined arbitrarily based on the criteria for the pediatric hydrocephalus diagnosed by means of pneumoencephalogram.<sup>20</sup> In addition to  $EI > 0.3$ , the Japanese guidelines emphasize the importance of DESH in the diagnostic criteria.<sup>19</sup> However, it is impossible or extremely difficult to diagnose iNPH only by the brain imaging data.<sup>39</sup> It has been well known that many elderly people show no signs and symptoms of iNPH, but their MRIs show typical findings of iNPH. These cases are known as AVIM (asymptomatic ventriculomegaly with features of iNPH on MRI),<sup>40</sup> which indicates a lack of correlation between the degree of ventricular enlargement and the severity of symptoms. Even now, it is still difficult to establish an evidence-based thresholds for the diagnosis of iNPH.<sup>29,39</sup> However, for the experienced neurosurgeons who have observed numerous normal head CT or MRI images in patients without any neurological abnormalities, such as those complaining of headaches or with mild head trauma, it

is not particularly difficult to qualitatively judge imaging findings such as anterior horn rounding, third ventricular ballooning, Sylvian fissure dilatation, and convexity subarachnoid space enlargement as indicative of abnormal CSF accumulation.<sup>29</sup> When elderly patients present with symptoms of iNPH, we recommend tap testing if these findings of abnormal CSF accumulation are present, even if the imaging does not meet the diagnostic criteria for iNPH and even if they have concomitant old cerebral infarction compatible with the diagnostic criteria of VaD.<sup>25</sup> If the tap test is positive, we perform VA shunt as first-line surgery. The two cases presented here meet these criteria.

### **What is Vascular Dementia?**

Extensive studies on AD<sup>4–6</sup> have disclosed the pathological findings and the pathomechanisms that have triggered the development of new therapeutic modalities.<sup>9–14</sup> As for VaD, four popularly used diagnostic guidelines have been published: ICD-10,<sup>41</sup> DSM-IV,<sup>42</sup> ASSTC,<sup>43</sup> and NINDS-AIREN.<sup>25</sup> Since the diagnostic criteria of VaD are different among these four guidelines and the cerebrovascular lesions are heterogeneous,<sup>25</sup> the number of cases that could be classified as VaD differed widely between the various diagnostic guidelines and the different criteria identify different frequencies and clusters of patients and they are not interchangeable<sup>16</sup>. Cholinesterase inhibitors and N-methyl-D-aspartate receptor antagonists are listed.<sup>44</sup> However, their effectiveness may be mediated through their effects on concomitant AD, and currently there are no substantial approaches other than prevention. VaD has long been known and was initially considered as a cause of early dementia, associated with ischemic brain disorders.<sup>2</sup> Some reports suggest that VaD accounts for 25 to 40% of dementia cases.<sup>45</sup> However, in recent Japanese epidemiological survey of dementia in the elderly (65 years and older), VaD accounts for 18.9% of all dementia cases, making it the second most common cause of dementia after AD.<sup>3</sup> The NINDS-AIREN diagnostic criteria<sup>25</sup> are used for the diagnosis of VaD in epidemiological surveys. These criteria mention that gait disturbance and urinary incontinence are often present early in VaD. Furthermore, iNPH is mentioned as a differential diagnosis stating that “The triad of gait disturbances, urinary incontinence, and dementia resembles normal pressure hydrocephalus clinically.”<sup>25</sup> However, this aspect is rarely considered during the diagnostic process of VaD. Differential diagnosis between AD and iNPH is not particularly difficult based on medical history, symptoms, and neuroimaging findings.<sup>19</sup> However, as evident from the two cases presented here the differentiation between VaD and iNPH is not always easy. Therefore, it is possible that iNPH may be included within the category of VaD in epidemiological surveys of dementia.<sup>3,46</sup>

### **Considering Idiopathic Normal Pressure Hydrocephalus and Vascular Dementia As Causes of Dementia**

In epidemiological surveys of dementia, VaD is often reported as the second most common type of dementia after AD, with a frequency of 18.9 or 29.5% of all dementia

cases.<sup>3,46</sup> Although iNPH has been recognized as a treatable cause of dementia for a long time,<sup>19,28–32</sup> it is rarely listed as an independent cause in dementia epidemiological studies. Besides AD and VaD, numerous other conditions such as iNPH, head trauma, vitamin deficiencies, hypothyroidism, and alcohol dependence are mentioned as causes of dementia.<sup>26,27</sup> INPH is presumed to be included in the category of “Other” in dementia epidemiological surveys, with reported frequencies of 3.3<sup>3</sup> or 6.2%.<sup>46</sup> In a Japanese community-based study, the incidence of iNPH in the elderly population (65 years or older) fulfilling the image diagnostic criteria of Japanese guidelines<sup>36</sup> was 2.9%.<sup>47</sup> However, among elderly individuals who had iNPH symptoms and experienced symptom improvement with a VA shunt, less than 30% of cases fulfilled both the criteria of  $EI > 0.3$  and DESH.<sup>29</sup> Craven et al also reported that DESH was observed only in 30% of cases classified as probable iNPH.<sup>48</sup> Therefore, it is estimated that the incidence of elderly individuals who may have positive response to shunt surgery is approximately 3.3 times higher than the community-based study, that means approximately 9.6% of the elderly population (65 years and above) may positively respond to VA shunts. The estimated prevalence of dementia in individuals aged 65 and older was 22.5% (768 dementia cases out of 3,418 participants).<sup>3</sup> The frequency of cognitive impairment in iNPH has been reported to be 78 to 98%.<sup>19</sup> Even with the lowest estimate of 78% it can be inferred that approximately 10% of elderly dementia patients are attributed to iNPH fulfilling the imaging diagnostic criteria. When including cases that do not fulfil the imaging diagnostic criteria, iNPH-related dementia may account for approximately 33% of the causes of dementia in elderly individuals. It can be the second most common cause of dementia after AD. Recent study disclosed that the patients with iNPH-related dementia showed highly positive response to CSF shunt surgeries even if they had comorbidity of AD.<sup>49</sup> Taken these speculations and the surgical outcome, considerable portion of the patients with AD and VaD may possibly have the comorbidity of iNPH. As Martín-Láez et al pointed out, iNPH may be very underdiagnosed condition.<sup>50,51</sup>

## Conclusion

We reported two cases previously diagnosed as VaD who showed significant cognitive improvement by means of VA shunt. Authors suggest that VaD may be very rare except for strategic single infarct dementia and Binswanger’s disease. Not limited to VaD, when symptoms are suggestive of iNPH especially after hospitalization, we recommend considering the possibility of iNPH and performing a tap test regardless of adherence to the imaging diagnostic criteria specified in the guidelines, as evident from the above discussion the prevalence of iNPH may be extremely underdiagnosed.

### Ethical Approval

Institutional board approval was obtained, and consent from both patients and their family was obtained ensuring anonymity.

### Funding

None.

### Conflict of Interest

None declared.

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