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Olfactory Dysfunction, an Often Neglected Symptom of Hydrocephalus: Experience from a Case of Late-Onset Idiopathic Aqueductal Stenosis

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Keywords
Hydrocephalus · Late-onset idiopathic aqueductal stenosis · Hyposmia · Olfactory dysfunction · Aqueductal stenosis

Abstract
Disturbance of smell is often accompanied with common neurodegenerative diseases such as Parkinson's and Alzheimer's diseases. In addition, patients with head trauma, intracranial tumors, and hydrocephalus can also develop olfactory dysfunction, and some of which can improve with treatment of the underlying disease. In clinical practice, few patients complain of smell disturbances, thus olfactory dysfunction is often overshadowed by visible motor symptoms. Herein, we report a case of late-onset idiopathic aqueductal stenosis, a rare form of adult-onset hydrocephalus in which olfactory dysfunction and gait disturbance was markedly improved after endoscopic ventriculostomy. This case report is expected to make more physicians aware that hydrocephalus can cause olfactory dysfunction and that it can be corrected postoperatively. Furthermore, in addition to motor and neuropsychological function, olfactory function test might be useful for functional assessment before and after surgical treatment of hydrocephalus.

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Introduction

Olfactory dysfunction is defined as a reduced sensitivity or a difficulty in identifying odors. Acquired olfactory disorders are classified according to both anatomical and etiological origin. The most common causes of acquired olfactory dysfunction are sinus disease and upper respiratory tract infection, which has recently been highlighted as an early manifestation or sequelae of COVID-19 infection. On the other hand, olfactory impairment is widely known as a non-motor manifestation of age-related neurodegenerative diseases including Parkinson's disease (PD) and Alzheimer's disease (AD) [1]. Particularly, in patients with PD and related disorders, impaired olfaction has attracted much attention not only as a non-motor symptom in the prodromal phase of disease but also as a clue for differentiating atypical and secondary parkinsonism [1]. Among frequently encountered neurological disorders in clinical practice, patients with hydrocephalus may also have a dulled sense of smell in addition to the gait and cognitive disturbances. The clinical presentation of hydrocephalus, particularly normal pressure hydrocephalus (NPH), sometimes resembles to PD and AD, and even both can be comorbid, making an accurate diagnosis difficult [2]. Here, we report a case of late-onset idiopathic aqueductal stenosis (LIAS) with olfactory impairment and gait disturbance, which markedly improved after neurosurgical treatment.

Case Presentation

A 76-year-old right-handed woman was referred to our hospital with a chief complaint of progressive gait disturbance. Neurological examination on admission showed mild rigidity in the left upper limb and postural instability with a mildly broad-based, small-stepped gait (online suppl. Video 1; for all online suppl. material, see www.karger.com/doi/10.1159/000529532). Neuropsychological battery scores were generally well maintained, e.g., 29 points for mini-mental state examination, 26 points for Montreal cognitive assessment, and 16 points for frontal assessment battery. Although the patient was unaware of hyposmia, the score on the odor stick identification test for Japanese (OSIT-J) had dropped to 2 points (cut-off value <7) [1]. Cranial magnetic resonance imaging (MRI) revealed the marked enlargement of the lateral and third ventricles (Fig. 1a, b), whereas neither disproportionately enlarged subarachnoid-space hydrocephalus findings nor the imaging features of atypical/secondary parkinsonism were observed (Fig. 1c). Subsequent constructive interference in steady-state imaging confirmed aqueductal stenosis by abnormal membranous structures (Fig. 1d), which was accompanied by almost complete loss of cerebrospinal fluid (CSF) flow on cine MRI (Fig. 1e). These characteristic imaging findings led us to the diagnosis of noncommunicating hydrocephalus due to LIAS. Furthermore, the presence of mild parkinsonism, olfactory dysfunction, and slightly decreased uptake of striatal dopamine transporter imaging (Fig. 1f) suggested comorbid PD.

Ventricular CSF sampling was not performed and endoscopic third ventriculostomy (ETV) was done, considering the risk-benefit of performing the ETV procedure with a single tap. Successful fenestration in the floor of the third ventricle was confirmed by postoperative MRI (Fig. 2a), and CSF flow in the same area was observed by cine MRI (Fig. 2b). Neurological evaluation 2 months postoperatively showed a wider stride, improved gait speed, and no sign of parkinsonism; however, mildly flexed posture remained (online suppl. Video 2). Unexpectedly, the surgical treatment returned the OSIT-J score to the normal level (7 points), in addition to motor symptom improvement.

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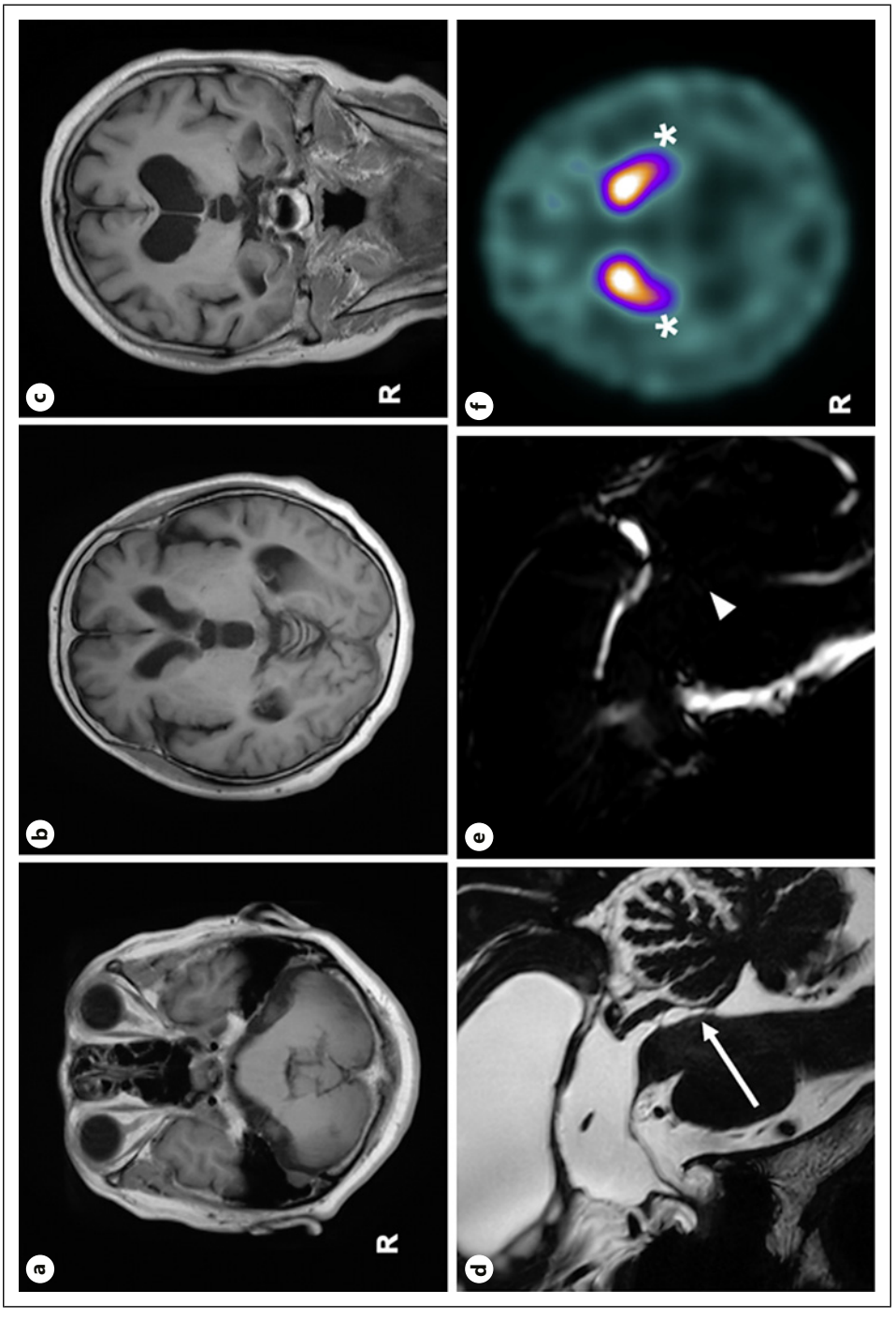

Fig. 1. T1-weighted cranial MRI. **a**, **b** The axial images of MRI show an enlarged third and lateral ventricle with normal size of fourth ventricle. No evidence of atypical or secondary parkinsonism. **c** Coronal T1-weighted imaging does not have a feature of DESH. **d** CISS imaging demonstrates the stenosis of the midbrain aqueduct (white arrowhead). **e** Phase-contrast cine MRI shows no cerebrospinal fluid flow in the same area (white arrow). **f** ^{123}I-ioflupane single-photon emission computed tomography (DAT scan™) shows slightly reduced uptake in the bilateral, dorsal parts of the striatum (white asterisk).

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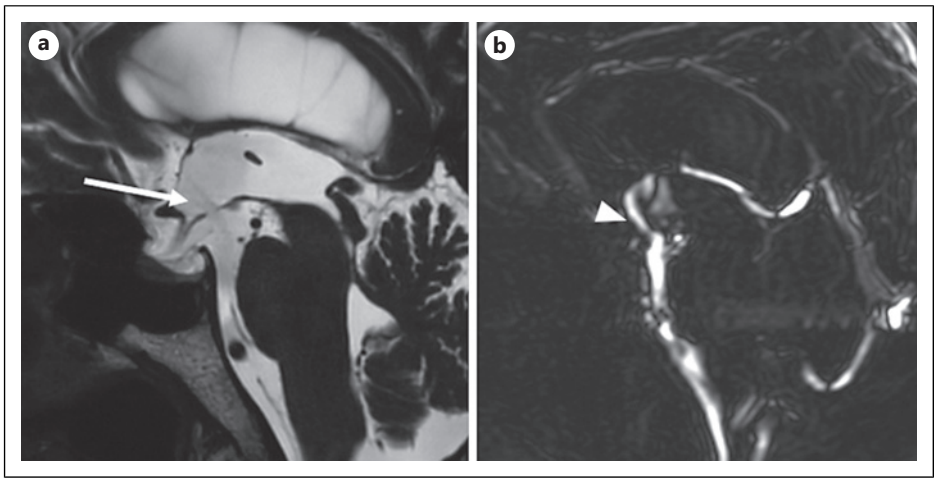

Fig. 2. a Postoperative MRI confirmed the fenestrated floor of the third ventricle (white arrow). **b** Phase-contrast cine MRI detects CSF flow in the same area (white arrowhead).

Discussion

Adult-onset hydrocephalus can develop secondary to other conditions, insidiously manifest due to congenital etiology, or idiopathic. Subarachnoid hemorrhage, NPH, intracranial tumors, and, to a lesser degree, aqueductal stenosis are the known causes. To the best of our knowledge, this is the first case of LIAS in which marked improvement in olfaction was confirmed postoperatively. LIAS is a rare form of adult-onset hydrocephalus and is characterized by triventricular enlargement due to an abnormal aqueductal membranous occlusion [3]. Its clinical manifestation includes headache, cognitive impairment, gait disturbance, and urinary incontinence, occasionally with parkinsonism, and rarely with olfactory dysfunction [4]. We initially suspected the coexistence of PD; however, most symptoms disappeared after the ETV, LIAS was finally conducted as the primary pathophysiology. Although the exact reason for slightly decreased presynaptic dopamine transporter density remains unclear in this patient, this finding is commonly observed in patients with idiopathic NPH [5].

Hydrocephalus is one of the less addressed causes of central olfactory dysfunction because both patient's and physician's attention is solely focused on motor and cognitive impairments that considerably interfere with daily life. Most reports of olfactory impairment associated with adult-onset hydrocephalus are associated with idiopathic NPH, which is a common condition in a large number of patients, but there is one paper addressing olfactory impairment due to aqueductal stenosis (Table 1) [2, 4, 6–8]. However, in our clinical experience, patients with cognitive decline are often unaware of their olfactory dysfunction probably due to pathological changes in the higher olfactory cortex and/or attention deficits. From the pathophysiological perspective, alteration of CSF flow/pressure dynamics may influence the olfactory function. For example, patients with idiopathic intracranial hypertension (IIH) may present with impaired smell sensation and a smaller volume of olfactory bulb [9]. Interestingly, olfactory dysfunction in patients with IIH could be recovered by intracranial pressure normalization [10]. Since patients with LIAS tend to show sustained high intracranial pressure, the ETV treatment performed in this case restores the physiological CSF circulation, thereby reducing intracranial pressure and normalizing olfactory sensation. It should be noted that olfactory dysfunction accompanied by NPH is often resistant to surgical treatment (Table 1) [2, 6]. Compared to NPH, obstruction of CSF flow is more obvious and localized in LIAS, which might be the reason why

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Table 1. Clinical characteristics of patients with adult-onset hydrocephalus with olfactory disturbance in the present case and the previous reports

	Present case	Leon-Sarmiento et al. [7] (2013)	Caminiti et al. [8] (2019)	Harrison et al. [4] (1974)	Podlesek et al. [6] (2012)	Passler et al. [2] (2017)
Number of patients	1	1	1	5	17	22
Age, sex	76, F	26, M	63, F	NA	66 (mean age), seven females	77.6 (mean age), eleven females
Diagnosis	LIAS	Juvenile NPH	Arrested hydrocephalus	Aqueduct stenosis	iNPH	iNPH
Cardinal symptoms	Hyposmia, rigidity, postural instability, gait disturbance	Anosmia, dementia, rigidity, tremor, hyperreflexia, laterocollis, gait disturbance	Anosmia, visual impairment, spastic quadriplegia, urinary urgency	Anosmia (bilaterally in two of five patients)	NA	NA
Olfactory tests used	OSIT-J	NA	SST and olfactory event-related potentials	NA	SST	UPSIT
Prognosis of olfactory impairment after treatment	Improved by ETV	NA	NA	NA	No improvement by VPS (n = 8)	No improvement with external lumbar drainage (n = 20) and VPS (n = 8)

LIAS, late-onset idiopathic aqueductal stenosis; OSIT-J, the Odor Stick Identification Test for Japanese; ETV, endoscopic third ventriculostomy; NPH, normal pressure hydrocephalus; NA, not available; SST, the Sniffin's Sticks Test; UPSIT, the University of Pennsylvania Smell Identification Test; iNPH, idiopathic normal pressure hydrocephalus; VPS, ventriculoperitoneal shunt.

hyposmia, in this case, showed a good response to the ETV procedure. Neurosurgeons treating patients with hydrocephalus should be aware of olfactory disturbance as well as motor symptom and cognitive dysfunction. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material.

Conclusion

Olfactory dysfunction can occur as a non-motor symptom of hydrocephalus and can be recovered by surgical intervention. This non-motor symptom may be underestimated because hydrocephalus is less emphasized by healthcare professionals as a cause of central olfactory dysfunction. In addition to the motor and neuropsychological examination, olfactory function test might be considered for the functional assessment before and after the surgical treatment in patients with hydrocephalus.

Acknowledgments

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Statement of Ethics

All procedures performed in studies involving human participant were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. This study protocol was reviewed and the need for approval was waived by Tohoku University Hospital Ethics Review Committee, Tohoku University. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Naoya Yamazaki and Takafumi Hasegawa: conceptualization, writing-original draft. Naoya Yamazaki, Takafumi Hasegawa, Kensuke Ikeda, Ako Miyata, Shin-ichiro Osawa, Kuniyasu Niizuma, and Shigenori Kanno: patient's care; Naoya Yamazaki, Takafumi Hasegawa, Kensuke Ikeda, Ako Miyata: data curation and investigation; Teiji Tominaga and Masashi Aoki: supervision; all authors: writing-review and editing.

Data Availability Statement

All data and material (Fig. 1, Fig. 2, and Table 1) supporting our findings have been provided. The data that support the findings of this study are openly available in "figshare" (Suppl video 1.mp4, DOI: 10.6084/m9.figshare.21965162; Suppl video 2.mp4, DOI: 10.6084/m9.figshare.21965174). Further inquiries can be directed to the corresponding author, Dr. Takafumi Hasegawa.

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