Secondary Amenorrhea Caused by Hydrocephalus Due to Aqueductal Stenosis
: Report of Two Cases

Amenorrhea is rarely presented as a manifestation of endocrinological disturbances in patients of chronic hydrocephalus. We describe two cases of secondary amenorrhea caused by hydrocephalus due to aqueductal stenosis. Two female patients of age 30 and 20 yr presented with amenorrhea and increasing headache. Magnetic resonance images revealed marked, noncommunicating hydrocephalus without any tumorous lesion. In one patient, emergent extraventricular drainage was necessary because of progressive neurological deterioration. Each patient underwent surgical intervention for the hydrocephalus-ventriculoperitoneal shunt and endoscopic third ventriculostomy. Both resumed normal menstruation continuing so far with further normal menstrual bleeding. These two cases and others reported in the literature indicated that the surgical intervention for hydrocephalus resolves amenorrhea in all the cases of amenorrhea due to hydrocephalus. The suspected role of the surgery is the correction of increased intracranial pressure, which is an important pathogenetic factor in the development of amenorrhea.

Key Words : Amenorrhea; Hydrocephalus; Ventriculoperitoneal Shunt; Ventriculostomy

INTRODUCTION

Endocrine dysfunction in hydrocephalus has been recognized for many years, characterized by precocious or delayed puberty, primary amenorrhea and somatic underdevelopment. Since the first operation in 1950 on a patient with amenorrhea and hydrocephalus (1), fewer than thirty patients with amenorrhea and hydrocephalus were reported (2-10). In addition, only three cases of secondary amenorrhea due to hydrocephalus have been described in the literature until now (5, 7). Secondary amenorrhea due to hydrocephalus by nontumoral cause is very rare, and only one case in which normal menstruation was induced after surgery has been previously reported (7).

CASE REPORTS

Case 1

A 30-yr-old woman with a history of headache and vomiting for one month was referred to emergency department with a sudden aggravation of headache and vomiting accompanied by mental deterioration. She had been suffering from upper respiratory tract infection 1 week prior to admission. On admission, she was drowsy. On physical examination, she was moderately obese, being 162 cm in height and weighing 67 kg. A discharge of clear, watery fluid from her nostril was detected, suggesting cerebrospinal fluid leakage. She had reached menarche at the age of 15 yr, and her subsequent menstrual cycles were 3 months in interval. She has been amenorrheic for 1 yr. Plain skull radiographs showed prominent convolutional markings suggesting chronic increased intracranial pressure (Fig. 1). A computed tomographic (CT) scan revealed prominent noncommunicating hydrocephalus. We performed emergent extraventricular drainage (EVD) into the right lateral ventricle and her mental state and symptoms of increased intracranial pressure improved postoperatively. Brain MRI with gadolinium enhancement obtained postoperatively showed marked dilatation of the third and lateral ventricles with a normal sized fourth ventricle, and there was no abnormal parenchymal lesion (Fig. 2). Preoperative endocrinological examination showed low FSH (3.4 IU/L), LH (4.2 IU/L), and low T₃ (25 ng/dL) but normal TSH (1.3 IU/L), thyroxine (5.3 μg/dL), and normal prolactin (7.9 ng/mL). Four
days later, EVD was replaced with ventriculoperitoneal shunt using the Medos Hakim programmable valve. Two days after the shunt, she experienced menstruation again and continues to be eumenorrheic for 18 months after the surgery. The cerebrospinal fluid (CSF) rhinorrhea was stopped 15 days after shunt. Postoperative concentrations of FSH (6.1 IU/L), LH (21.1 IU/L), and T3 (111 ng/dL) were increased with normal TSH (1.89 IU/L) and thyroxine (6.7 μg/dL).

Eight months later, she was readmitted to the hospital because of headache and a decreased level of consciousness. She experienced minor traffic accident one day before admission. It was just fender bender and she was in the passenger seat. The plain skull radiography and CT showed a both frontal tension pneumocephalus. An emergency burr hole in the right frontal area with evacuation of the air was performed, improving the neurological status of the patient. She was discharged with just valve pressure adjustment. Six months later, she was readmitted because of headache and vomiting. CT showed pneumocephalus on both lateral ventricle and she was managed conservatively. Multiple bony defects were revealed in the cribriform plate of the ethmoidal bone by CT scan using 2-mm sections. We recommended transcranial repair of the fistula, but she did not want to undergo any procedure. Fortunately there was no further episode of rhinorrhea during follow-up period.

Case 2

A 20-yr-old woman presented with a 2-month history of gait disturbance. Headache, vomiting and urinary incontinence were developed 6 weeks prior to admission. She had been relatively healthy until she was 16-yr-old when she began to show the symptoms of depression and a decline in her school performance. Five months prior to admission, she had psychiatric medication under the diagnosis of depression and schizophrenia. On admission, she appeared to be dull and mentally retarded. On physical examination, she weighed 63 kg and was 150 cm tall. She had reached menarche at the age of 15 yr, following which she had been
eumenorrheic. Amenorrhea was shown for recent 3 months. Preoperative endocrinological examination showed low FSH (4.6 IU/L), LH (7.8 IU/L), and T₃ (60 ng/dL) but normal TSH (1.19 IU/L) and thyroxine (4.9 μg/dL) with minimal elevation of prolactin (30.5 ng/mL). Plain skull radiographs showed multiple erosive change of both skull vault with erosion of the dorsum sella suggesting chronic increased intracranial pressure (Fig. 3). Brain MRI with gadolinium enhancement revealed prominent obstructive hydrocephalus secondary to aqueductal stenosis with diffuse thinning and elevation of the corpus callosum, and no tumorous lesion was demonstrated (Fig. 4). Endoscopic third ventriculostomy via right frontal burr hole was performed. Improvement of urinary incontinence and gait disturbance were noted immediately. Two months after surgery, she experienced menstruation again and continues to be eumenorrheic for 18 months after surgery. Psychiatric disturbance was also improved and psychiatric medication was not necessary. Postoperative endocrinological evaluation showed an increase of concentrations of T₃ (140 ng/dL) with normal TSH (1.7 IU/L) and thyroxine (10.8 μg/dL), and no change of FSH (4.7 IU/L) and LH (7.7 IU/L).

DISCUSSION

Congenital aqueductal stenosis (CAS) is the most common cause of aqueductal narrowing. Despite its congenital origin, the alteration of cerebrospinal fluid dynamics can remain compensated and undiagnosed for several years, and symptoms related to hydrocephalus due to CAS may not occur until adult life (11). The ventricular system is usually very large as shown in these two cases.

Chronic hydrocephalus in adult is associated with visual disturbance, papilledema, dementia, or ataxia (2). However, endocrine dysfunctions are uncommon and rarely revealing. Villani et al. (11) reported that the endocrine dysfunctions are evident in 28% of the CAS cases. The most common manifestations of endocrinological disturbances are hypothalamic-hypophyseal-gonadal axis impairment such as pre-
Secondary Amenorrhea and Hydrocephalus

Secondary amenorrhea and hydrocephalus is not well-known (3, 5, 7, 12-14). Jawadi et al. (5) described secondary amenorrhea in a patient with hypothalamic astrocytoma. They suggested that the increased intracranial pressure due to hydrocephalus rather than the hypothalamic tumor caused an inhibitory effect on the hypothalamus-pituitary-ovary axis at the level of the hypothalamus. Coenegracht et al. (3) postulated that the increased intraventricular pressure caused a functional disturbance only in the gonadotropin releasing hormone (GnRH) secreting neurons in the ventral hypothalamus and not in the median eminence, leading to a relative GnRH deficiency. Relative GnRH deficiency theory has been supported by several authors using GnRH infusion test (9) or 24-hr LH surge analysis (7). According to previous reports, it could be suggested that if the third ventricle is dilated progressively in chronic hydrocephalus, GnRH release is disturbed only in the ventral hypothalamus without the disturbance of GnRH production elsewhere, subsequently causing relative deficiency of GnRH and resulting in amenorrhea.

Amenorrhea is an unusual manifestation of endocrinological disturbances in patients of chronic hydrocephalus, but all of the patients who had undergone surgical treatment reported to achieve normal menstruation. Thus, all women with hypothalamic amenorrhea should be investigated for the presence of any intracranial cause, and brain MRI is preferred, if available. In case of amenorrhea with hydrocephalus, surgical intervention for the hydrocephalus should be attempted to relieve the intracranial pressure and therefore to induce cyclic menstruation.

On the contrary, hydrocephalus is also linked with neuropsychiatric symptoms. Intellectual deterioration is predominant and the mood and character disturbances are very rare (2). The clinical manifestations of psychiatric disturbances generally take precedence over the endocrine symptoms as shown in Case 2. Psychiatric symptoms in Case 2 are also improved with surgical intervention for the hydrocephalus. With the increasing availability of computed tomography, more patients with neuropsychiatric symptoms associated with hydrocephalus may be reported in the future, and therefore the clinical features and mechanisms will be clarified in more details.

Rhinorrhea can occur without any history of trauma or cranial surgery, which is called spontaneous or nontraumatic. Spontaneous CSF fistulae are associated with congenital bone defects, tumors, infection, hydrocephalus, and acquired pitholes in the skull base (15). Some patients with spontaneous CSF fistulae have associated unrecognized hydrocephalus or increased intracranial pressure. Several cases of pneumocephalus associated with shunted hydrocephalus have been reported in patients with a history of aqueductal stenosis. Thinning of the cranial floor and dor-
13. Ekblom M, Ketonen L, Kuuliala I, Pelkonen R. Pituitary function in patients with enlarged sella turcica and primary empty sella syndrome. Acta Med Scand 1981; 209: 31-5.

14. Kulali A, Baykut L, von Wild K. Relationship between chronic raised intracranial pressure and empty sella presenting hormonal disturbances. Neurol Res 1990; 12: 99-102.

15. Landreneau FE, Mickey B, Coimbra C. Surgical treatment of cerebrospinal fluid fistulae involving lateral extension of the sphenoid sinus. Neurosurgery 1998; 42: 1101-5.

16. Villarejo F, Carceller F, Alvarez C, Bencosme J, Perez Diaz C, Goldman L, Pascual A. Pneumocephalus after shunting for hydrocephalus. Child's Nerv Syst 1998; 14: 333-7.