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Hydrocephalus Due to Diffuse Villous Hyperplasia of the Choroid Plexus

—Case Report—

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Abstract

An 8-month-old female presented with hydrocephalus caused by cerebrospinal fluid (CSF) overproduction due to bilateral choroid plexus enlargement, which was clinically diagnosed as diffuse villous hyperplasia of the choroid plexus, but differentiation from bilateral choroid plexus papilloma was difficult. She initially underwent ventriculoperitoneal shunt surgery, but developed marked retention of ascites. Therefore, the peritoneal end of the shunt was removed for external drainage, but excessive CSF (1,500 ml/day) was collected. Computed tomography and magnetic resonance imaging revealed marked symmetric enhancement of the choroid plexuses in the bilateral lateral ventricles. Thallium-201 chloride single-photon emission computed tomography showed pronounced uptake on both early and delayed images, and good washout. CSF examination revealed no abnormalities such as atypical cells, and a ventriculoatrial shunt was inserted, achieving good control of the hydrocephalus.

Key words: choroid plexus, hyperplasia, hydrocephalus, cerebrospinal fluid overproduction, ventriculoatrial shunt

Introduction

Diffuse villous hyperplasia of the choroid plexus (DVHCP) is a rare condition involving enlargement of the entire choroid plexus, which remains histologically normal, resulting in severe hydrocephalus due to cerebrospinal fluid (CSF) overproduction. DVHCP must be differentiat-

ed from the rare occurrence of bilateral choroid plexus papilloma (CPP), but discrimination between the two diseases still presents problems. We treated a patient under a diagnosis of DVHCP based on clinical findings, but differentiation from bilateral CPP was difficult due to the lack of pathological specimens.

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Case Report

An 8-month-old female was brought to our hospital as an emergency case from a local hospital due to an acute increase in her head circumference, tightness of the lower limbs, and poor sucking ability on September 30, 2009. She was born in distress by Caesarian section on the 4th day of the 34th week of pregnancy in December 2008. Computed tomography (CT) showed intraventricular bleeding and hydrocephalus, but she was discharged after 1 month, and she was observed on an outpatient basis. After about 2 months, she developed tightness of the lower limbs, gradually lost energy, and demonstrated poor sucking reflex, so she was taken to another hospital. Since emergency magnetic resonance (MR) imaging revealed marked hydrocephalus, she was transported to our hospital.

On admission, her head circumference was 49.5 cm ($> +2$ standard deviation), compared to 43.1 cm 1 month earlier. The anterior fontanelle was tense, and sunset phenomenon, tightness of the lower limbs, and scalp vein distention were observed. Heart rate, respiratory rate, blood pressure, and body temperature were normal. Blood examination showed no abnormalities in any parameter including electrolytes, renal function, and liver function. CT revealed marked ventricular dilation and periventricular lucency (Fig. 1).

Emergency ventriculoperitoneal (VP) shunt surgery was performed. The surgical procedure was completed

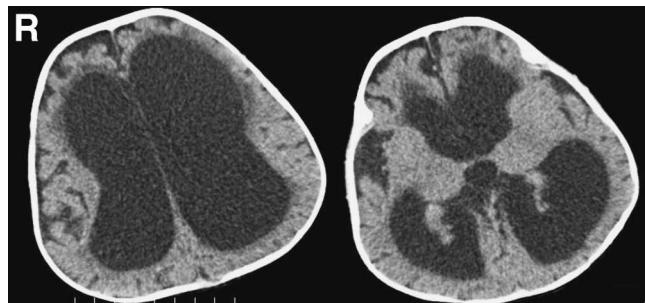


Fig. 1 Computed tomography scans on admission showing marked ventricular dilation and periventricular lucency.

without problems. On the day following the operation, marked abdominal distension occurred. Abdominal CT revealed massive accumulation of free fluid in the abdominal cavity (Fig. 2). We considered that her peritoneum could not adequately absorb the CSF, and removed the peritoneal end of the shunt to allow external drainage. The initial pressure was established at 100 mm above the patient's external acoustic meatus. Since 200 ml CSF/hour drained from the external acoustic meatus, intermittent clamping was performed to prevent excessive outflow. However, 200 ml CSF/hour continued to drain. CSF examination showed no abnormal values or atypical cells.

CT and MR imaging, both with contrast medium, showed prominent enhancement of the symmetrically enlarged bilateral choroid plexuses (Fig. 3). Thallium-201 chloride single-photon emission computed tomography (Tl SPECT) revealed marked uptake on both early and delayed images and good washout with a negative retention index (Fig. 4). After 2 weeks, her general condition worsened, with hyponatremia, methicillin-resistant *Staphylococcus aureus* pneumonia, and meningitis, prompting performance of a tracheotomy. However, improvement was observed after antibiotic administration intravenously and into the CSF. The diagnostic significance of the Tl SPECT was unclear at this point, but

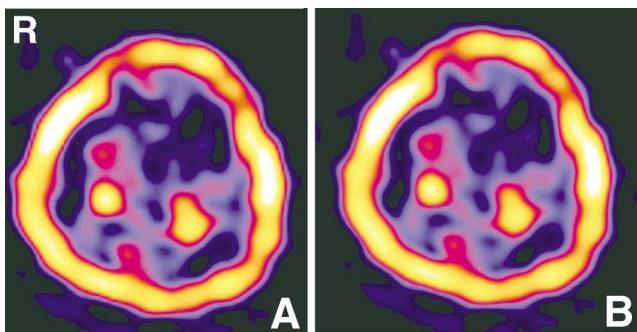


Fig. 4 Thallium-201 chloride single-photon emission computed tomography scans showing marked uptake (tumor to non-tumorous brain ratio) on both early (A: right 11.81, left 13.68) and delayed images (B: right 3.08, left 3.09), and negative retention index (right -73.91, left -77.4), suggesting good washout.

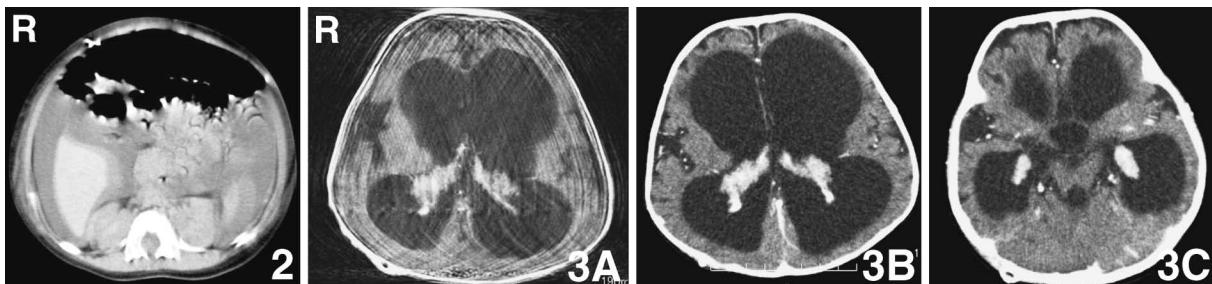


Fig. 2 Abdominal computed tomography scan on the day after the first operation revealing massive free fluid in the peritoneum.
Fig. 3 T₁-weighted magnetic resonance image (A) and computed tomography scans (B, C) with contrast medium showing no mass lesion, but the markedly enhanced bilateral choroid plexuses.

Table 1 Cases of bilateral choroid plexus papilloma and diffuse villous hyperplasia of the choroid plexus (DVHCP)

Author (Year)	Age at initial procedure	Radiographical features	Initial (and 2nd) procedures	Last procedure	Clinical diagnosis	Histological findings
Gudeman et al. (1979) ¹²⁾	3 yrs	SE	VPS, VAS	resection	papilloma	papilloma
Welch et al. (1983) ²²⁾	7 yrs	SE	VPS	resection	DVHCP	NCP
Bucholz and Pittman (1991) ³⁾	29 mos	SE	VPS	EC	DVHCP	NCP
Hirano et al. (1994) ¹³⁾	7 yrs	SE	VPS	resection	DVHCP	NCP
Britz et al. (1996) ²⁾	3 mos	SE	VPS	VAS	DVHCP	no
Philips et al. (1998) ¹⁶⁾	14 mos	SE, CF	VPS	EC, VPS	DVHCP	NCP
Fujimura et al. (2001) ¹¹⁾	10 mos	SE, lobular	VPS, VAS	resection	papilloma	papilloma
Erman et al. (2003) ⁹⁾	3 yrs	ASE, lobular	resection	(resection)	papilloma	papilloma
D'Ambrosio et al. (2003) ⁷⁾	3 mos	SE	VPS	resection	DVHCP	NCP
Fujimoto et al. (2004) ¹⁰⁾	20 mos	SE	VPS	resection	DVHCP	NCP
Aziz et al. (2005) ¹¹⁾	11 yrs	SE	VPS (at 2 mos)	resection	DVHCP	NCP
Tamburini et al. (2006) ¹⁹⁾	24 mos	SE	VPS	EC, resection, VPS	DVHCP	NCP
Iplikcioglu et al. (2006) ¹⁴⁾	5 yrs	SE	VPS	VAS	DVHCP	no
Smith et al. (2007) ¹⁸⁾	15 mos	SE	VPS	resection, VPS	DVHCP	NCP
Warren et al. (2009) ²¹⁾	8 days	SE, irregular	VPS	resection, VPS	DVHCP	NCP
Nimjee et al. (2010) ¹⁵⁾	6 mos	ASE, CF	VPS, VAS	resection	papilloma	papilloma
Cataltepe et al. (2010) ⁵⁾	9 days	SE	VPS, EC	resection, VPS, VAS	DVHCP	NCP
Present case	8 mos	SE	VPS	VAS	DVHCP?	no

ASE: asymmetrical enlargement, CF: cyst formation, EC: endoscopic coagulation, NCP: normal choroid plexus, SE: symmetrical enlargement, VAS: ventriculoatrial shunt, VPS: ventriculoperitoneal shunt.

DVHCP was the most likely diagnosis based on the CT, MR imaging, and CSF findings. After resolution of the meningitis, a ventriculoatrial (VA) shunt was inserted.

She was transferred to the previous referring hospital, and has been followed up on an outpatient basis. Her intracranial pressure has been well controlled. No morphological changes were observed in the bilateral plexuses on follow-up CT 6 months after the operation.

Discussion

DVHCP was first reported by Davis⁸⁾ in 1924 before the introduction of CT, and only 18 patients with hydrocephalus caused by CSF overproduction due to bilateral choroid plexus enlargement have been reported, including findings employing imaging techniques (Table 1).^{1-3,5,7,9-16,18,19,21,22)} In most patients, VP shunt surgery was performed but failed, resulting in marked ascites. This suggests difficulty in establishing the diagnosis of this disease in the initial stage.

Bilateral CPP is characterized by asymmetric enlarged choroid plexuses^{9,15)} which tend to be separated into lobules,^{9,11)} and cyst formation in a few cases.¹⁵⁾ However, the enlarged choroid plexuses were symmetric and resembled DVHCP on imaging in some cases,¹²⁾ enabling diagnosis only after pathological examination. Most patients diagnosed with DVHCP^{1-3,5,7,10,13,14,16,18,19,21,22)} showed symmetric choroid plexus enlargement, but some exhibited irregular enlargement²¹⁾ or cyst formation.⁶⁾ In addition, no pathological findings were available in 3 patients including our patient, so the diagnosis of DVHCP was based on imaging findings.^{3,14)} Differential diagnosis is possible based on imaging findings,¹⁴⁾ and VA shunt surgery is the simplest and most appropriate choice,²²⁾ considering the

risks of complications of resection such as hemianopsia, nystagmus, and bleeding during the operation due to the rich blood flow in the choroid.^{15,19)} Indeed, 3-year follow-up examination showed good control of hydrocephalus and absence of morphological changes in the choroid plexus in previous patients.^{2,14)} Similar results were obtained in our patient, although the follow-up period was only 6 months. We also evaluated other options (biopsy or resection), but selected VA shunt without biopsy and resection, considering the risks of shunt failure due to bleeding-related increase in the CSF protein level when a shunt becomes necessary, infection due to long-term external drainage, and electrolyte abnormalities due to the removal of a large volume of CSF from the body.³⁾ However, pathological findings may be needed to establish the diagnosis.^{9,11)} Initial VA shunt was subsequently followed by tissue resection and pathological examination due to the development of complications such as thrombosis and infection, resulting in the diagnosis of bilateral CPP.^{11,15)} In most previous patients, the diagnosis of DVHCP was established based on the histological findings.^{1,3,5,7,10,13,16,18,19,21,22)} However, pathological examination suggested DVHCP on the tissue surface but CPP in the lobular lesion, confounding the pathological diagnosis of DVHCP in one case.¹¹⁾

Tl SPECT observed symmetric, marked uptake in the bilateral choroid plexuses on both early and delayed images and good washout, showing a negative retention index in our patient (Fig. 4). Tl SPECT in a patient with unilateral lateral ventricular CPP observed marked uptake in the CPP on the affected side on both early and delayed images and a retention index of -0.15, indicating moderate washout, but no uptake in the choroid plexus on the unaffected side.¹⁷⁾ Although the CT and MR imaging find-

ings suggested DVHCP in our patient, CPP remains a possibility. Therefore, long-term follow-up observation is necessary despite the absence of morphological changes after 6 months.

DVHCP may progress to CPP and finally to choroid plexus carcinoma (CPC), suggesting the importance of measuring the MIB-1 index.⁷⁾ The MIB-1 index is nearly 0% in the normal choroid plexus, 0.2–17.42% in CPP, and 4.14–29.74% in CPC.^{4,6,20)} The MIB-1 index was 4% in a previous case,⁷⁾ and 3% (left) and 0.5% (right) in another case,⁵⁾ suggesting the transition period from DVHCP to CPP in both patients. The pathological condition may have reflected this transition from DVHCP to CPP in patients with histological findings differing between specimen sites,¹¹⁾ atypical imaging findings for pathological findings,^{16,21)} or uptake on T1 SPECT despite DVHCP suggested by CT and MR imaging, as in our patient.

In the majority of patients^{2,3,5,7,10–16,18,19,21,22)} including ours, VP shunt surgery was performed first, but failed due to marked ascites. Subsequently, resection or endoscopic coagulation was performed in most patients to inhibit CSF production, followed by radical or shunt surgery.^{1,3,5,7,10–13,15,16,18,19,21,22)} The advantage of these procedures is that histological diagnosis is possible, so CPP is not overlooked. However, the histological findings may differ between sites, which causes confusion.¹¹⁾ In addition, there are risks of neurological complications,²²⁾ and adverse effects of invasiveness, such as bleeding.²¹⁾ On the other hand, a method in which excessive CSF is returned to the systemic circulation using a VA shunt has been proposed,¹⁴⁾ which is noninvasive and straightforward, but whether the direct return of a large volume of CSF to the systemic circulation is appropriate remains questionable. The most important disadvantage is that definite histological diagnosis cannot be established. In our patient, excessive CSF was also directly returned to the systemic circulation using a VA shunt, but long-term follow-up observation is necessary.

The present and previous cases of hydrocephalus caused by CSF overproduction due to bilateral choroid plexus enlargement considered to be DVHCP suggest that a full disease description, diagnostic criteria, and treatment methods have not yet been established, requiring further studies.

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