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Case report

Cerebral fluid overproduction in the absence of tumor or villous hypertrophy of the choroid plexus

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Abstract. A case of cerebrospinal fluid overproduction in a 2.5-year-old child is reported. The rate of cerebrospinal fluid production was more than four times the expected amount. There was no evidence of tumor or villous hypertrophy of the choroid plexus. The child was successfully treated with a ventriculoatrial shunt.

Key words: Cerebrospinal fluid – Cerebrospinal fluid shunts – Choroid plexus – Papilloma.

Hydrocephalus is a pathologic condition characterized by accumulation of cerebrospinal fluid (CSF) in the ventricular system. In the majority of cases it results from impaired reabsorption or obstruction to flow. It may also result from overproduction. Although Russell has stated that there is no proof of this [20], numerous case reports have documented high levels of CSF production in patients with papillomas or hemangiomas of the choroid plexus [11, 13, 19]. Laurence has also suggested that villous hypertrophy of the choroid plexus may result in overproduction [15].

We present a case of CSF overproduction in which there was no evidence of tumor or villous hypertrophy of the choroid plexus.

Case report

C.P. (CHP 42-48-84) is a 2.5-year-old white child born of a 39-week pregnancy to a 28-year-old white woman, gravida 1, para 0. At the age of 6 months, macrocephaly was noted during an evaluation for developmental delay. A computed tomographic (CT) scan demonstrated hydrocephalus (Fig. 1). A ventriculoperitoneal (VP) shunt was inserted on 6 June 1983. This was followed by symptomatic ascites. Six months after insertion, the shunt was externalized because of this problem. The ascites promptly resolved. On 15 December 1983, a VP shunt was reinserted. Two months later, the ascites returned and the shunt was again externalized. On this occasion the externalization was complicated by a coagulase negative staphylococcal infection. The infection resolved after treatment with intravenous nafcillin and intrathecal methicillin. On 13 March 1984, a VP shunt was again inserted. This was again followed by symptomatic ascites. The VP shunt was removed and an external ventricular drain was placed. The ascites again resolved, but the patient became febrile. This was traced to a *Serratia marcescens* bacteremia. The same organism was obtained from the CSF. At this point the patient was transferred to the Neurosurgery Service of Children's Hospital of Pittsburgh. A 6-week course of antibiotic therapy with intravenous and intrathecal gentamycin was necessary to eradicate the infection. External ventricular drainage (EVD) was continued throughout this period.

The daily output of cerebrospinal fluid from the ventricular drain was more than four times the expected amount. The cerebrospinal fluid outputs for selected 8-h intervals at a pressure of 0 cm of water with respect to the foramen of Monro are shown in Table 1. Because of persistent ventriculomegaly and a decreased level of consciousness, the pressure of the ventricular drainage system was reduced to −5 cm of water. Typical cerebrospinal fluid outputs at this pressure are shown in Table 2. At this time, small extra-axial colelctions of fluid were noted on a CT scan (Fig. 2). Because of this, the ventricular drainage pressure was progessively increased to +15 cm of water with respect to the foramen of Monro. This had no adverse effect on her clinical status. Selected cerebrospinal fluid outputs during this period are shown in Table 3. At a pressure of +15 cm of water, the extra-axial fluid collections resolved without change in the degree of ventriculomegaly.

Multiple examinations of the cerebrospinal fluid over the 6-week course of ventricular drainage revealed a protein that ranged

Table 1. Cerebrospinal fluid output at a pressure of 0 cm of water

Time	28 March 1984	30 March 1984	3 April 1984
07.00–15.00	704 cc	514 cc	839 cc
15.00–23.00	654 cc	448 cc	763 cc
23.00–07.00	506 cc	680 cc	870 cc

Table 2. Cerebrospinal fluid output at a pressure of −5 cm of water

Time	5 April 1984	6 April 1984	12 April 1984
07.00–15.00	826 cc	960 cc	638 cc
15.00–23.00	900 cc	878 cc	768 cc
23.00–07.00	760 cc	786 cc	538 cc

Table 3. Cerebrospinal fluid output at pressures up to +15 cm of water

Time	15 April 1984 (+5 cm H_2O)	17 April 1984 (+15 cm H_2O)
07.00–15.00	630 cc	438 cc
15.00–23.00	648 cc	715 cc
23.00–07.00	682 cc	472 cc

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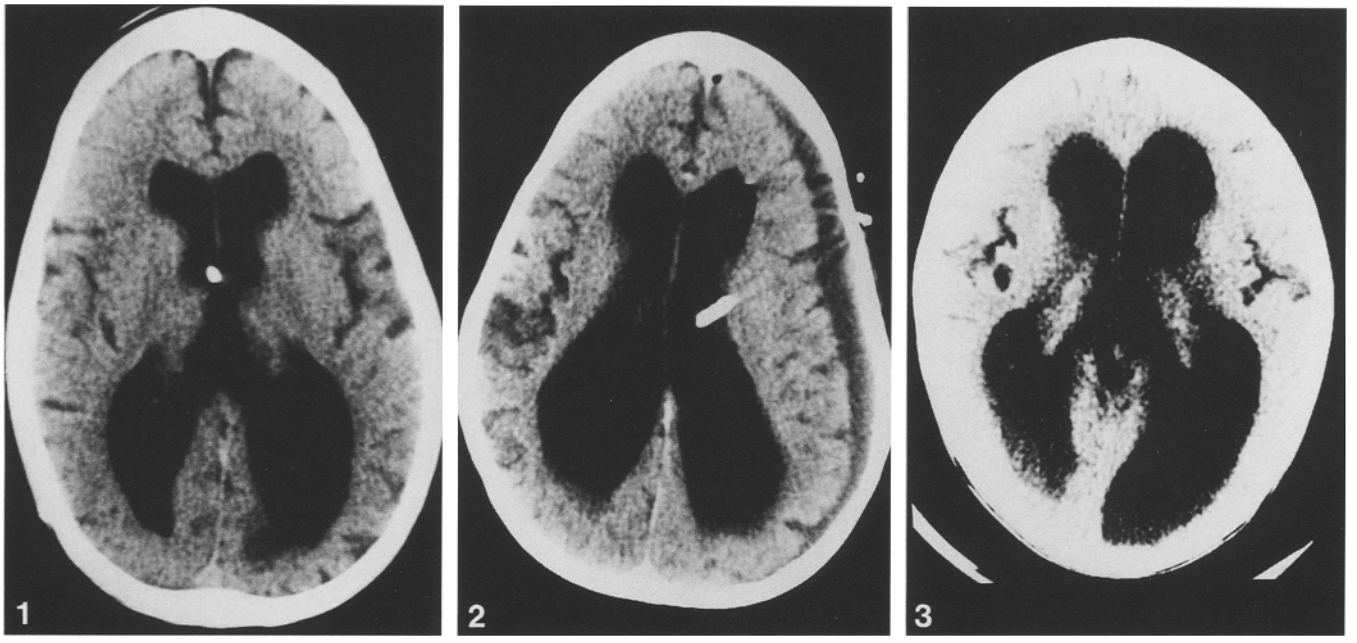

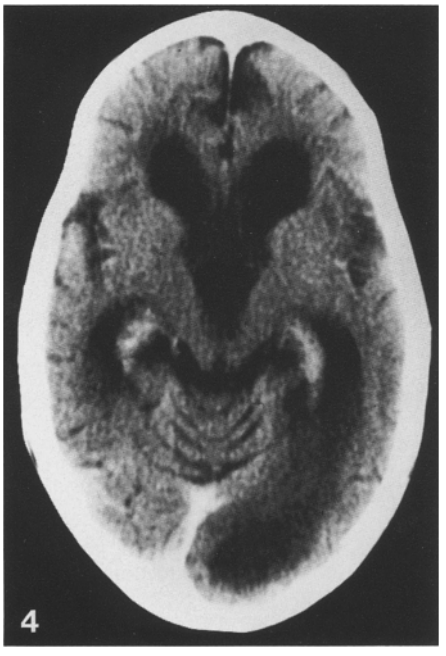

Fig. 1. CT scan at 6 months of age demonstrating significant ventriculomegaly

Fig. 2. CT scan demonstrating an extra-axial fluid collection over the left cerebral convexity

Fig. 3. CT scan with contrast enhancement showing no evidence of choroid plexus abnormalities

Fig. 4. CT scan 11 months after insertion of a ventriculoatrial shunt showing a significant decrease in ventricular size

from 4–70 mg%. The average red cell count was 18 cells/mm^3. Biweekly checks of electrolytes including sodium and potassium levels were within normal limits. The ventricular drain was changed on a weekly basis using the procedure described by Friedman and Vries [23]. A contrast-enhanced CT scan with 5-mm cuts showed no evidence of choroid plexus abnormalities (Fig. 3).

On 8 May 1984, a ventriculoatrial shunt was performed using a Hakim system (Cordis Corporation). The openening pressure of the valve was 56–90 mm of water. The ventricular catheter was inserted at the level of the coronal suture using the technique described by Vries [22]. Prior to insertion, an endoscope was used to inspect the choroid plexus of the right lateral ventricle. There was no evidence of tumor or hypertrophy. Her postoperative course was unremarkable. Her level of consciousness gradually returned to normal. A CT scan on 27 June 1984 showed a decrease in ventriculomegaly. On follow-up examination 11 months after surgery, her developmental milestones were normal. A CT scan on 2 April 1984 showed further decrease in the size of her ventricles.

Discussion

The predominant site for cerebrospinal fluid production is the choroid plexus of the lateral and III ventricles [8]. Reabsorption takes place over the cerebral hemispheres via the arachnoid villi. Most modern studies have shown that the interstitial fluid makes a minimal contribution to cerebrospinal fluid production from either the brain [3, 4] or the spinal cord [2, 17, 18]. This is challenged by the study of Sato, which suggests that a significant production takes place within the spinal compartment [21]. Their experimental design, however, does not take into account the effect of cerebrospinal fluid entering from above.

Cerebrospinal fluid production is an energy-dependent process involving the active transport of sodium and potas-

sium ions. The volume of cerebrospinal fluid production per unit weight of choroid plexus is constant across a wide variety of species [7, 8]. The average rate of production in humans using the cisterna magna perfusion method is 0.33 ml/min ± 0.02 ml/min [6].

Overproduction of cerebrospinal fluid has been reported with unilateral and bilateral choroid plexus papillomas [5, 11, 13, 19]. Villous hypertrophy as a cause of overproduction has also been described by Laurence [15]. He reported a case of his own and reviewed six cases from the literature. In each case, the degree of hypertrophy of the chloroid plexus was marked. Whether these lesions represent hypertrophy, or neoplasia remains unclear. Baar and Galinda, whose case was included in the Laurence review, described their case as a choroid plexus papilloma [1].

The child reported in this paper had four separate contrast enhanced CT scans (General Electric 9800) during the course of her treatment. Two of these studies utilized 5-mm sections. There was no evidence of tumor or enlargement of the choroid plexus. The choroid plexus of the right lateral ventricle was also inspected with an endoscope at the time of shunt placement. The choroid plexus was unremarkable. The only abnormalities seen were sparse patches of exudate consistent with the resolving phase of a ventricular inflammatory process.

In Eisenberg's case of choroid plexus papilloma, a rate of cerebrospinal fluid production of 1.4 ml/min was measured using a perfusion technique [11]. Fairburne found an output of 500–960 ml/day using a drainage system at zero pressure level [13]. In our case, the rate of cerebrospinal fluid output averaged 1.4 ml/min (range 1.12–1.82 median 1.38) during the 6-week externalization period. This probably underestimates true production because the effect of pressure-dependent absorption is not known. The etiology of overproduction in our patient remains obscure. The results of the CT scans and the endoscopic inspection of the choroid plexus appear to rule out tumor and villous hypertrophy.

Increased cerebrospinal fluid production has been noted in rats and monkeys following sympathectomy [10, 16]. The magnitude of the increase has been only 30%, however. The magnitude of the increase in our patient was more than 400%. Moreover, there was no clinical evidence suggesting a loss of sympathetic tone. The only exogenous accelerator of cerebrospinal fluid production that has been identified is cholera toxin [12]. The mechanism of acceleration appears to be related to an increase in cyclic AMP [14]. Experiments using vasopressin and a variety of agents that increase the turnover of sodium ions did not accelerate the production of cerebrospinal fluid [9].

It is possible that the blood flow through the choroid plexus in our patient was incresed as a result of inflammation. Unfortunately, there is no solid evidence linking increased blood flow in the choroid plexus to increased cerebrospinal fluid production. The overproduction also seems to have preceded the ventricular inflammatory process. This leaves us without a plausible hypothesis to explain the striking clinical findings in this patient.

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