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Acquired aqueductal stenosis in preterm infants: an indication for neuroendoscopic third ventriculostomy

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Abstract *Object:* The object of this study is to demonstrate the delayed occurrence of aqueductal stenosis in preterm infants who have suffered from intraventricular hemorrhage (IVH) and to try to explain the mechanisms of this stenosis. *Method:* From January 1996 to June 2002, 1,046 premature infants were admitted to our institution. Thirty-six neonates suffered from grade 3 or 4 intraventricular hemorrhage (Papile grading), of whom 16 died. Twenty patients survived and a ventriculoperitoneal shunt was inserted in 7 infants. Four patients underwent a neuroendoscopic third ventriculostomy. Follow-up was carried out, twice a month during the first 2 months and subsequently twice a year. *Conclusion:* In 2 children NTV was an effective treatment for hydrocephalus with an average follow-up of 29 months. The specific pattern concerning these patients is the long delay before obstructive hydrocephalus and the visualization of de novo obstruction with MRI. The biological explanation must be investigated.

Keywords Premature newborn · Intraventricular hemorrhage · Hydrocephalus · Neuroendoscopy · Aqueductal stenosis · Acquired obstructive hydrocephalus · Transforming growth factor β1

Introduction

Infants delivered at less than 35 gestational weeks (GW) are at high risk of intraventricular hemorrhage (IVH). In the neonatal period, this hemorrhage may be complicated with communicating hydrocephalus in 15% of cases [6]. This is commonly treated with ventriculoperitoneal shunts. This type of communicating hydrocephalus is due to either arachnoiditis of the basal cisterns or sclerosis of Pacchioni granulations.

We describe an unusual presentation of hydrocephalus secondary to acquired aqueductal stenosis. This has not been described before in the premature population.

Acquired aqueductal stenosis in the preterm infant population raises the possibility of neuroendoscopic third ventriculostomy (NTV). We report 4 patients of less than 35 GW who suffered from neonatal IVH with delayed obstructive hydrocephalus. The supposed mechanisms of this unusual type of hydrocephalus are discussed.

Materials and methods

This retrospective study was conducted at one center from January 1996 to June 2002.

One thousand and forty-six premature infants delivered before 35 GW were admitted to the neonatal intensive care unit of the American Memorial Hospital of Reims. Thirty-six neonates suffered from grade 3 or 4 intraventricular hemorrhage (Papile grading) [14]: 16 died (15 aged less than 26 GW, 1 aged 29 GW). Twenty patients survived and a ventriculoperitoneal shunt was placed in 7 infants. Four patients underwent a neuroendoscopic third ventriculostomy. The decision to perform endoscopic ventriculostomy was based on radiographic data. Radiologic diagnosis of obstructive hydrocephalus was established by sagittal T1 or T2 MRI sequences and fourth ventricle morphology on axial images (3 patients). For 1 patient, only CT images were available. The normal size of the fourth ventricle, lateral ventricle dilatation and the huge downward expansion of the third ventricle floor are the radiologic indicators of obstructive hydrocephalus considered in this study. Preoperative aqueductal flow sequences were not available.

Neuroendoscopic treatment was considered successful when no other procedure was required for hydrocephalus. Gestational

Table 1 Patients' clinical characteristics (*IVH* intraventricular hemorrhage)

	Gestational age (weeks)	Birth weight	Grading IVH	Lumbar puncture	DVE	Fibrinolysis	Age/NTV	Results	Follow-up
Case 1	26	1,200 g	2	Yes	0	0	7 months	Success	9 months
Case 2	33.5	1,400 g	3	Yes	1	1	20 months	Success	38 months
Case 3	28	1,200 g	4	Yes	1	1	6 months	Failure	Lost
Case 4	35	2,430 g	3	Yes	1	0	36 months	Failure	12 months

age, birth weight, age at neuroendoscopic treatment, initial hemorrhage grading, therapeutic modalities and interval between birth and neuroendoscopic treatment are reported in Table 1. Follow-up was carried out by a pediatric neurologist and a pediatric neurosurgeon, twice a month during the first 2 months and subsequently twice a year.

Results

In the immediate postnatal period, the 4 children presented with communicating hydrocephalus. They were treated with CSF withdrawal in 4 cases, external shunt in 1 case, and internal shunt in 1 case. Gestational age at birth ranged from 24 to 35 GW. Fulminant progressive obstructive hydrocephalus evolved after 6–36 months (average 17 months). Clinical signs of obstructive hydrocephalus were progressive macrocephaly (3 cases) and symptoms consistent with elevated ICP (1 case). No morbidity or mortality was observed after neuroendoscopic third ventriculostomy. The ventriculostomy was considered successful in 2 patients and the follow-up was 10 months in 1 and 48 months in the other. In the remaining 2 patients, treatment was ineffective after 1 week (case 4) and after 6 weeks (case 3).

Discussion

Intraventricular hemorrhage (IVH) is a well-known complication of premature delivery and low birth weight [8, 10, 14, 22]. Initial hemorrhage occurs, usually in the germinal matrix of one side, adjacent to the head of the caudate nucleus. Immaturity of the ependyma and vessels is cited as an explanation for the high frequency of intraventricular bleeding at this age [8, 22, 23].

The clinical presentation of intraventricular hemorrhage depends on the extent of bleeding. According to Papile grading, this hemorrhage is subdivided into [14]:

Grade 1: hemorrhage limited to the germinal matrix
Grade 2: germinal matrix hemorrhage extending into the lateral ventricle without distension
Grade 3: intraventricular hemorrhage associated with ventricular distension
Grade 4: grade 3 with parenchymal hemorrhage beyond the germinal matrix

Hydrocephalus usually appears 3–4 weeks after the IVH [8]. According to the literature, hydrocephalus is due to an intense inflammatory reaction in the subarachnoid space. This phenomenon results in the thickening of the basal cisterns and an obstruction of the arachnoid villi. These lesions result in communicating hydrocephalus [8, 16, 17, 22]. With regard to communicating hydrocephalus, some authors make a distinction [15] between obstruction of the basal cisterns and obstruction of the arachnoid villi. The latter is apparently the cause of real communicating hydrocephalus [15].

In this study, we described an obstructive hydrocephalus with acquired aqueductal stenosis. The pattern particular to these patients is the long delay before obstructive hydrocephalus; 17–25 months is the average time before the hydrocephalus required treatment. In patients who successfully underwent NTV this delay was 13.5 months.

Our hypothesis is that acquired aqueductal stenosis may be the consequence of a progressive obstruction. According to Sarnat [18], the ependyma does not regenerate at any age and it reacts to injury with a few stereotypical responses. The tearing of the epithelium by ventricular distension carries discontinuities between cells, filled with subventricular astrocyte processes. This glial response can be extensive [18], leading to the formation of nodular gliosis. Such gliosis in the periaqueductal area may be responsible for progressive obliteration. Fibrous intraventricular scarring, secondary to IVH, may contribute to this obstruction [9]. This gliotic reaction develops over time, which could explain the delay in acquired aqueductal stenosis occurrence. Similar scars and nodular gliosis can be found in infectious diseases such as mumps [20] with acquired stenosis [9, 13]. In the 2 successfully treated children, obstruction was observed on sagittal MRI with wide opening of the upper extent of the aqueduct, while obstruction was visible on the inferior part (see Fig. 2).

Biological elements may also explain this progressive obstruction. Transforming Growth Factor Beta 1 is a cytokine, which is stored in the platelets and released in the CSF following IVH. It belongs to the super-family of Transforming Growth factors, which play a critical role in the regulation of various cellular functions [11, 12]. TGFB 1 has the biological property of up-regulating the genes for extra cellular matrix proteins such as fibronectin and laminin. It is involved in scar formation and fi-

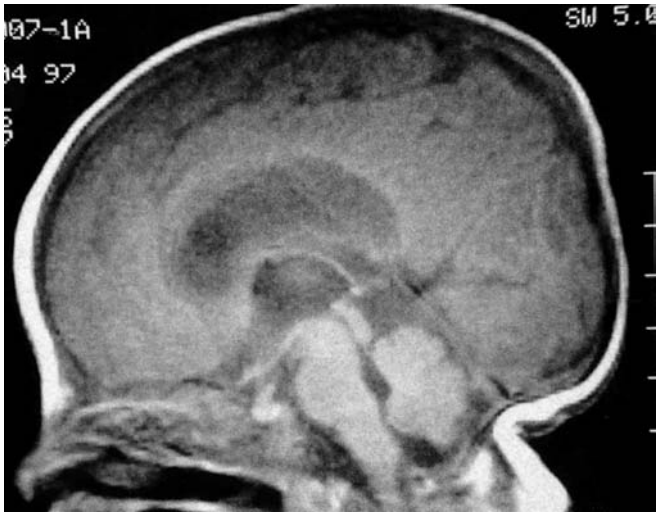

Fig. 1 MRI in the neonatal period shows a patent aqueduct without dilatation of the upper part

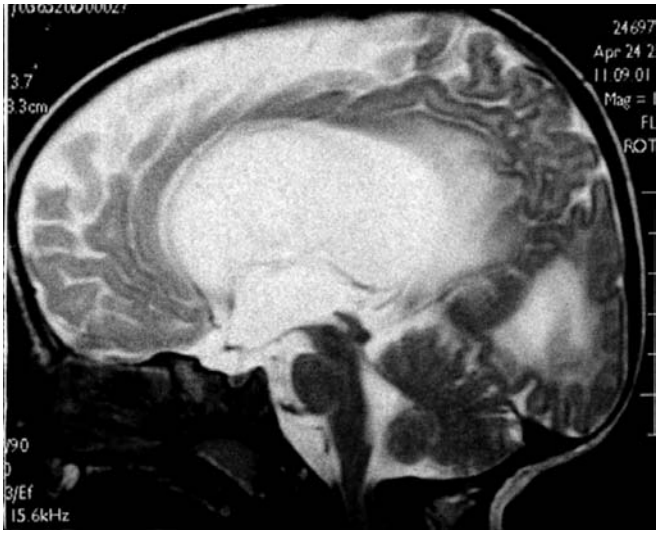

Fig. 2 MRI before NTV (at the age of 7 months). Obstructive hydrocephalus. MRI shows a marked dilatation of the upper part of the aqueduct with obstruction in the inferior part

brotic disease [2, 12, 19, 22]. According to Whitelaw [22], TGFB 1 is virtually undetectable in normal neonatal cerebral spinal fluid (CSF). TGFB 1 concentration increases after bleeding or post-hemorrhagic ventricular dilatation. He argues that TGFB1 stimulates the production of extracellular matrix proteins around the brain stem and in the subarachnoid space. This "scar tissue" blocks the exit of the fourth ventricle or the reabsorption channels [23]. By extension, it may be supposed that this scar could also block the lumen of the aqueduct.

We state that this stenosis is "acquired". Indeed, in the neonatal period, several lumbar punctures were effective at reducing ventricular dilatation in our patients. Transfontanellar echography showed marked dilatation of the entire ventricular system and in 1 case (case 2) MRI in the neonatal period showed a patent aqueduct (Fig. 1) that later disappeared (Fig. 2).

In our study, 2 out of 4 neuroendoscopic procedures were effective. Failures were probably due to the initial selection of patients. In case 3, NTV failed 6 weeks after the procedure. At this time we had to choose between a second NTV or shunting and we decided to place a shunt. Case 4 presented with clinically significant intracranial hypertension 30 months after the insertion of a ventriculoperitoneal shunt. The decision to perform an endoscopic third ventriculostomy was based on CT, which revealed a marked dilatation of the ventricles with a less marked dilatation of the fourth ventricle. The diagnosis was obstructive hydrocephalus and NTV was performed. It failed 1 week later. This example indicates the utility of MRI with Cine study before NTV. In this population of infants, transtentorial asymmetry on CT is not sufficient to determine the type of hydrocephalus and therefore the optimal treatment. According to some authors, efficiency of NTV in preterm neonates is not convincing [3, 4, 5, 6] and the successful procedure rate is close to 10%. Despite these poor results, Buxton advocates carrying out NTV first to try to avoid a shunt [4]. In our preterm patients, the situation is different. Treatment occurs later. At this age, the results of NTV are excellent [1, 7, 21] with a success rate close to 90%. Thus, we think that in cases of acquired aqueductal stenosis in older preterm infants, NTV must be recommended as the first treatment.

Conclusion

Our practice suggests that acquired mechanical obstruction of the Sylvian aqueduct must be borne in mind by neurosurgeons involved in preterm hydrocephalus. This hydrocephalus occurs later in the evolution of IVH. Cine MRI is necessary to ascertain the diagnosis and to optimize the treatment. In our opinion, NTV must be carried out in such conditions as to avoid shunt insertion and therefore shunt complications. However, the long-term benefits must be assessed by longer follow-ups.

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