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CLINICAL ARTICLE - BRAIN TUMORS

Repeated assessment of suspected normal pressure hydrocephalus in non-shunted cases. A prospective study based on the constant rate lumbar infusion test

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Abstract
Background Only a few reports have been published on the natural history of non-shunted patients suspected of having NPH. The aim of this study is to follow up a group of such cases.
Methods It was possible to follow up 27 patients who had not been qualified for shunting after the primary diagnosis. An assessment of Hakim's triad was performed, together with an analysis of radiological parameters and the results of lumbar infusion tests (LITs), both on admission and at the later date (on average, after 5.6 months). All parameters were analyzed with respect to periventricular lucency (PVL), atrophy, type of NPH, and the age of the patients.
Results There were no deteriorations and six patients improved. Those who were over 50 and who had no PVL or secondary NPH tended to improve more frequently. Significant improvement of dementia was noted ($p = 0.042$) in all cases, and in the group of patients without PVL ($p = 0.04$). The size of the ventricles did not change significantly. The values of the resistance to outflow (R), elastance (E), and ICP remained stable.
Conclusions Analysis of our series revealed that the patients suspected of having NPH who had not been qualified for shunting did not deteriorate, while some of them even improved significantly as far as the level of dementia was concerned. As the CT and LIT parameters remained stable, there were no indications for repeating these examinations, at least within the period of nearly 6 months, which followed the primary diagnosis.

Keywords Normal pressure hydrocephalus · Non-shunted hydrocephalus · Lumbar infusion test · Repeated hydrodynamic test · Intracranial pressure–volume reserve

Introduction

Normal pressure hydrocephalus (NPH) remains an enigmatic entity, notwithstanding intensive research. The current theory of NPH formation involves consideration not only of simple disturbances of cerebrospinal fluid (CSF) outflow but also of vascular compliance with the redistribution of vascular pulsations [7]. To date, the availability of proper diagnostic methods which take this new theory into account is limited. In patients with suspected NPH, diagnosis is still usually based on clinical symptoms (Hakim's triad), assessment of radiological examinations (CT, MRI), and hydrodynamic tests. However, there is a group of patients who account for about 30 % of all cases of suspected NPH—both idiopathic and secondary chronic—in whom the size of the enlarged ventricles fulfills the radiological criterion of hydrocephalus, but in whom Hakim's triad is incomplete or has elements that are doubtful or not very severe, while the tap test is negative and the hydrodynamic tests reveal low resistance to CSF outflow (R) or the occurrence of only slight disturbances. Such findings do not allow these patients to be considered as candidates for CSF diversion. Assessment of outcome in shunted series of patients has been well documented in the literature [5, 39, 42]. There have been only a few published reports on the

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natural history of NPH patients [3, 6, 9, 14, 24, 26, 29, 34] and one double-blind randomized trial has yet to be completed [38]. The outcome in non-shunted cases of NPH has been described in no more than seven studies (comprising a total of 120 patients) [34, 40] and in these cases the method and time of follow-up, or even its advisability, remains unclear. Other important questions are: do these patients deteriorate (and, if so, how many?) and do any of them improve without shunting? [40].

The aim of our study has been to follow up a group of non-shunted cases of suspected NPH and to compare the relevant parameters of the lumbar infusion test (LIT), together with their neurological status and their radiological measurements.

Materials and methods

There were 36 patients suspected of suffering from NPH who had not been qualified for shunting after the primary diagnosis and who were therefore included in the prospective study. It was possible to follow up 27 of them. Of the remaining nine patients, eight refused to participate in the second investigation, and did not declare any deterioration in their general and mental condition. Another patient died because of a pulmonary artery embolism. In accordance with the protocol, all patients included in the prospective study were informed about the date of the second investigation well in advance—by mail—and were also reminded later by telephone. Their relatives were also contacted. Within the investigated group of patients were 14 females and 13 males (age range, 22–74, mean, 51.3 years of age). In 12 cases, secondary communicating hydrocephalus was diagnosed as a result of SAH (six cases) or as a consequence of intracranial tumor surgery (three cases), meningitis (two), or trauma (one). In 15 patients, idiopathic NPH was suspected. The duration of symptoms varied from 1 to 36 months (giving a mean 7.5 months). Four patients (15 % of those analyzed) declared co-morbidities such as nephritis, anemia, ischemic heart disease, and arterial hypertension. All of these patients received appropriate treatment and remained stable. Patients signed individual agreements before taking part in the study.

An assessment of the clinical symptoms of hydrocephalus, the analysis of radiological parameters, as well as the LITs were performed and examined twice: on admission, and at 5 to 7 months later (on average 5.6 months after the first assessment). The level of the severity of symptoms was assessed by means of the scale proposed by Sahuquillo, Rubio et al. [28], in which walking ability, incontinence, and dementia were individually assessed on a scale of 1 to 5 (5 being the best). Assessment of dementia and qualification for a given category of cognitive function impairment was carried out independently by a qualified psychologist. The results were later added together (Table 1).

Radiological assessment was based on CT. Planimetric measurements were carried out in order to verify the radiological criteria of hydrocephalus. Any ventricular enlargement that was greater than accepted as normal was considered as hydrocephalus: ventricular index > 0.8, Evans ratio > 0.3, third ventricle diameter > 7 mm, bicaudate index > 0.2. Cerebral atrophy and periventricular lucency (PVL)—whether present or not—were assessed by a qualified radiologist. Cerebral atrophy was considered to be present when the enlargement of cerebral sulci (at the lateral fissure and the convexity of the brain) significantly exceeded the level that was acceptable as being normal for the age of the patient. PVL, if present in their characteristic location, was always distinguished from leukoaraiosis (Fig. 1).

The LITs were performed using one spinal needle (18 gauge) introduced into the lumbar subarachnoid space under local anesthesia. The needle was connected to a transducer (giving the pressure measurement) and a syringe was filled with a saline solution for the infusion. Once the calibration of the CSF measuring system and the basal CSF pressure (ICP_B) were determined, the infusion pump was started. The infusion rate (Q_i) was 2 ml/min.

The *ICP* response was measured with a piezoelectric transducer, sampled at 20 Hz, and stored on a standard PC equipped with an analogue-to-digital converter.

In-house software [25] written in C++ language for Windows was used off-line to fit the dynamic response *ICP(t)* to the observed data using the following equation:

$$ICP(t) = P_O + \frac{(ICP_B - P_O)(ICP_e - P_O)}{(ICP_B - P_O) + (ICP_e - ICP_B)\exp\left[\frac{E \cdot Q(ICP_e - P_o)}{(ICP_e - ICP_B)}t\right]} \quad (1)$$

where:

ICP(t)	is the fitted response of ICP to an infusion starting at time t = 0
ICP_b [mmHg]	is the measured baseline (‘opening’) ICP before the beginning of the infusion
Q_i	is the given (=2.0[ml/min]) infusion rate of mock CSF.
ICP_e [mmHg]	is the estimated asymptotic end-plateau value of *ICP* at infinitely long infusion time
E [1/ml]	is the estimated elastance index of the cerebrospinal system
P_0 [mmHg]	is the estimated offset parameter in compliance characteristics

The outflow resistance can be established from the above parameters as:

$$R_{out} = \frac{ICP_e - ICP_B}{Q_i} \quad (2)$$

Table 1 The assessment of the clinical symptoms of hydrocephalus

Gr.	Gait	Cognitive functions	Continence
1	Bedridden	Vegetative	Both urinary and fecal incontinence
2	Ambulation is possible with help	Severe dementia	Continous urinary incontinence
3	Independent walking possible, but is unstable	Important memory problems with severe behavior disturbances	Sporadic urinary incontinence
4	Abnormal, but stable	Memory problems reported by patient or family	Urinary urgency
5	Normal	Only cognitive disturbances are found by specific tests	No sphincter dysfunction

In turn, the intracranial compliance can be calculated as a function of intracranial pressure using the formula:

$$C(ICP) = \frac{1}{E \cdot (ICP - P_O)} \quad (3)$$

In the above equations, there are three parameters (ICP_e, E, P_0) that can be fitted simultaneously by a non-linear minimization algorithm. However, the offset pressure P_0, may be also assessed from the relation between the amplitude of *ICP(t)* fluctuations *AMP* and its current mean value:

$$AMP = k \cdot (ICP - P_O) \quad (4)$$

where *k* denotes the gradient of the regression line. The *AMP* was estimated as the maximum peak of Fourier transform corresponding to the frequency of the heartbeat.

A knowledge of P_0 permitted to reduce the number of unknown parameters of Eq. (1) to two. Additionally, when P_0 was constrained, the estimation of *E* was much more reproducible. This is because the parameters *E* and P_0 are not independent. For any value of susceptibility, *C*, there is an infinite number of pairs *E* and P_0 fulfilling the relation $E = 1/(C^*(ICP - P_0))$, resulting directly from Eq. (3). Therefore, fixing of P_0 stabilizes the value of *E*.

After finishing the examination, a tap test was performed in each case, with a diversion of about 30 to 40 ml of CSF.

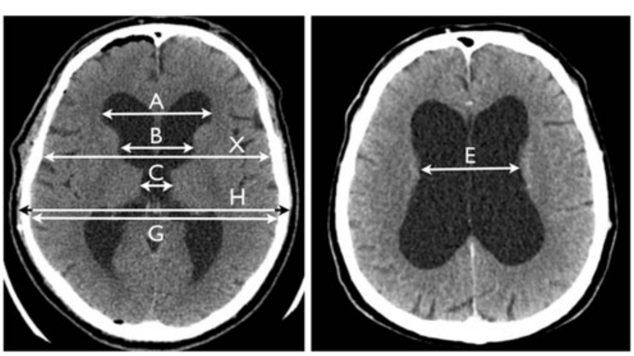

Fig. 1 Planimetric measurements of the ventricles. The parameters are considered to be pathological when they exceed the given values: ventricular index (A + B + 3C + E) / H > 0.8; Evans ratio A / G > 0.3; width of the third ventricle >7 mm; bicaudate index B / X > 0.2

Neurological, radiological, and hydrodynamic parameters were analyzed in all cases, and also in selected subgroups of patients. The following criteria were chosen in order to perform analysis: PVL (yes, no), atrophy (yes, no), the type of NPH (idiopathic, secondary), the age of the patients (under 50, over 50).

For a statistical comparison of the relevant data, the dependent variables, Student's *t* test was performed. We used it to confirm or reject (at the significance level of 0.05) the null hypothesis of no change between radiological, neurological, or LIT parameters tested twice. In order to calculate the *p* value of all compared groups of data, we used the standard procedures provided by the Microsoft Office Excel spreadsheet. The level of significance for all statistical tests was set to $p < 0.05$.

Results

Clinical symptoms

During the first assessment, the sum of the level of symptoms (LS) varied from 4 to 15 points, with a mean of 12.2. Three out of 27 patients presented with severe Hakim's syndrome (4, 6, and 7 points on the given scale), which meant that they were unable to lead an independent existence. In the follow-up, the level of symptoms varied from 4 to 15 points, a mean of 12.8. Six patients improved—two of them spectacularly. There were no deteriorations as far as the Hakim triad was concerned. When total values were assessed, there was no overall statistically significant difference in the level of symptoms. However, patients who were over 50, and who had no PVL or secondary NPH tended to improve more frequently. An analysis of the subgroups of patients revealed that statistically significant improvement of dementia was noted ($p = 0.042$) in all cases and also in the group of patients with no PVL ($p = 0.04$). In other selected subgroups there were no statistically significant changes in the clinical condition (Tables 2 and 3).

Radiological measurements

Cerebral atrophy was observed in 14 cases (52 %) and PVL in nine (33 %). These two parameters remained unchanged in the follow-up. The mean values of the Evans ratio, the ventricular index, the bicaudate index, and the width of the third ventricle were almost the same in both assessments, with no statistically significant differences. In two cases, however, the size of the ventricles was slightly smaller in the follow-up as compared with the initial assessment. The size of the ventricles did not change significantly in the subgroups of patients (Table 4).

The lumbar infusion test

An analysis of the parameters of the LIT revealed that the mean values of R remained unchanged (7.5 mmHg/ml/min). Also, in all subgroups, mean R values and mean cerebral elastance (E) values did not change significantly in the primary and follow-up examinations. In the vast majority of patients, the values of E were elevated, being over 0.18, which indicated a limited intracranial volume–pressure reserve. In almost all cases, pre-infusion ICPs were normal in both assessments (Table 5 and Fig. 2).

Tap tests, which were performed at the end of each LIT, did not result in an unequivocal improvement in every case.

Discussion

Signs

Non-shunted patients who are suspected of suffering from NPH are rarely followed up [6, 9, 14, 24, 26, 29, 30, 34]. It is unclear whether they should be checked at all, and if so, when this should be done. In previous reports, assessments have been performed after various periods of time, ranging from 3 months to 7.2 years [40]. We arbitrarily assumed that a period of 5-7 months after the first assessment was long enough to expect changes in patients' neurological, radiological, and hydrodynamic status. In general, there were no statistically significant changes as far as the Hakim triad was concerned. However, an analysis of the subgroups revealed that a significant improvement of dementia was noted, and also the patients who were over 50 and who had no PVL or who had been suspected of having secondary NPH tended to improve more frequently as far as continence and dementia were concerned. Six patients improved and in two of them the improvement was spectacular. Some differences might be due to the fact that a quantitative assessment of the elements of Hakim's triad is to a certain extent subjective.

Nevertheless, we observed that during the observation time, nearly a quarter of the cases in our series improved and none deteriorated. The Swallow et al. series [34] is the only one in which all 18 unshunted patients remained clinically unchanged 3.5 months after the first assessment, but only an unchanged neurological status served as the inclusive criterion for that study. Hughes et al. [14] have found that 50 % of non-shunted cases remained stable for up to 36 months and suggest caution in recommending the shunt procedure. An analysis of the remaining six studies comprising a total of 106 cases [6, 9, 24, 26, 29, 30] revealed that a small number of patients might have improved without shunting, while some remained unchanged. As far as idiopathic NPH is concerned, most of the patients showed measurable deterioration in the three months following the initial assessment. We may therefore conclude that non-shunted patients must be followed up. Nevertheless, surgery should not be considered in those patients in whom indications for shunting are not convincing. Despite very technically advanced valves, the overall complication rate is still high and accounts for between 18 and 21 % of all shunted cases [21], while shunt failures account for about 15 % of all operated cases [23]. Co-morbidity is a statistically significant predictor of the quality of outcome in patients undergoing shunt therapy [18]. A recent systematic review [39] shows

Table 2 Changes of the neurological status of the patients

Parameter	LS 1 points	LS 2 points	*p* value	Improvement (% points)	No. of cases	No. of improved	Improved (%)
PVL	11.2	11.3	0.343	0.9	9	1	11.1
No PVL	12.7	13.5	0.07	6.3	18	5	27.8
No/small atrophy	12.7	13.5	0.182	6.3	13	3	23.1
Significant atrophy	11.7	12.1	0.164	3.4	14	3	21.4
Idiopathic NPH	11.8	11.9	0.162	0.8	15	2	13.3
Secondary NPH	12.7	13.8	0.09	8.7	12	4	33.3
Age 50-	13.2	13.8	0.336	4.5	13	1	7.7
Age 50+	11.2	11.9	0.05	6.3	14	5	35.7
All cases	12.2	12.8	0.056	4.9	27	6	22.2

LS level of symptoms

Table 3 Changes of the neurological status: the analysis of the subgroups of the patients

Parameter	Gait 1	Gait 2	*p* value	Cont. 1	Cont. 2	*p* value	Dem.1	Dem.2	*p* value
PVL	3.78	3.78	1.00	3.89	3.67	0.35	3.67	3.67	1.00
No PVL	4.22	4.50	0.14	4.39	4.72	0.10	4.06	4.28	**0.04**
No/small atrophy	4.15	4.46	0.22	4.38	4.69	0.22	4.15	4.31	0.17
Significant atrophy	4.00	4.10	0.34	4.00	4.20	0.19	3.70	3.90	0.17
Idiopathic NPH	3.93	3.93	0.99	4.07	4.13	0.33	3.80	3.87	0.33
Secondary NPH	4.25	4.67	0.14	4.33	4.83	0.10	4.08	4.33	0.08
Age 50-	4.50	4.80	0.34	4.50	4.70	0.34	4.20	4.30	0.34
Age 50+	3.60	3.80	0.17	3.90	4.20	0.10	3.60	3.90	0.08
All cases	4.07	4.26	0.13	4.19	4.44	0.07	3.93	4.07	**0.042**

Bold data are statistically significant at $p < 0.05$

Gait 1 first assessment, *Gait 2* follow-up, *Cont.* continence, *Dem.* dementia

that the combined common complication rate is lower (8.2 %) than in past assessments. Nevertheless, patients should not be qualified for valve implantation when the likelihood of improvement after shunting is low or the risk of surgery outweighs the benefits.

Radiological assessment

In our group, mean values of all the radiological parameters were almost the same in both assessments, with no statistically significant differences. This could indicate that the observation time was too short to detect any changes in the CT in this particular group of patients, or that we assessed a group in which hydrocephalus was stable. In two cases, the size of the ventricles even decreased slightly in the follow-up. The difference, however, was very small, perhaps owing to the procedure dictated by the particular method of planimetric measurement. Indeed, planimetric measurements are not usually considered to be an ideal method for the estimation of ventricular volume in NPH cases, particularly as far as the Evans index is concerned [37]. Volumetric methods are recommended for differentiating between NPH and cerebrovascular disease (CVD) [10] because they provide a more accurate assessment of the true ventricular size as well as the size of the other intracranial CSF compartments [35, 37]. Recently, however, it has been established that the planimetric method—with measurements being made independently by a resident of neurosurgery and radiology, together with a qualified neurosurgeon and radiologist and also a medical student—proved to be both reliable and reproducible [27]. We may nevertheless conclude that in both assessments the radiological parameters were most stable as compared with the LIT and the neurological data. Another practical conclusion in cases of suspected NPH concerns the time at which a controlled CT should be performed. According to our observations, repetition of CT during the first 6 months appears to be unnecessary and even inadvisable.

The lumbar infusion test

The constant rate LIT is most often used in clinical practice for the dynamic assessment of CSF outflow. Other tests, i.e., the lumboventricular test and the constant pressure infusion test, are only rarely carried out [18, 33]. The LIT allows us to

Table 4 The values of planimetric measurements (CT) in the first and second assessment

Parameter	EI1	EI2	*p* value	III 1	III 2	*p* value	BI1	BI2	*p* value	VI1	VI2	*p* value
PVL	0.36	0.36	0.991	12.70	13.00	0.347	0.26	0.26	0.347	1.076	1.078	0.347
No PVL	0.39	0.38	0.331	11.92	11.62	0.331	0.28	0.27	0.178	1.145	1.121	0.165
No/small atrophy	0.40	0.40	0.337	11.88	11.88	0.999	0.30	0.30	0.337	1.18	1.16	0.337
Significant atrophy	0.35	0.35	0.336	12.45	12.26	0.671	0.24	0.24	0.369	1.07	1.06	0.390
Idiopathic NPH	0.36	0.36	0.999	12.91	12.91	0.999	0.26	0.26	0.999	1.08	1.08	0.999
Secondary NPH	0.40	0.40	0.173	11.26	11.03	0.190	0.28	0.28	0.190	1.173	1.14	0.190
Age 50-	0.40	0.40	0.999	11.55	11.55	0.999	0.27	0.27	0.999	1.164	1.164	0.999
Age 50+	0.36	0.36	0.865	12.76	12.57	0.671	0.27	0.26	0.192	1.082	1.054	0.190
All cases	0.38	0.38	0.167	12.18	12.08	0.663	0.27	0.27	0.185	1.12	1.11	0.185

EI Evans index, *III* width of the third ventricle, *BI* bicaudate index, *VI* ventricular index

Table 5 The values of LIT parameters in the first and second assessment

Parameter	R_1	R_2	*p* value	% of change	E_1	E_2	*p* value	% of change	P_{01}	P_{02}	*p* value	% of change
PVL	7.8	6.9	0.2	-11.5	0.23	0.23	0.992	0.0	4.4	6.2	0.112	40.9
no PVL	7.4	7.9	0.112	6.8	0.236	0.203	0.253	-14.0	7.5	7.8	0.79	4.0
no/small atrophy	7.8	8.2	0.369	5.1	0.24	0.217	0.546	-9.6	8.5	7.7	0.906	-9.4
sign. atrophy	7.2	7.0	0.591	-2.8	0.229	0.208	0.426	-9.2	4.6	6.8	0.024	47.8
idiopathic NPH	7.3	7.4	0.821	1.4	0.248	0.232	0.538	-6.5	6.73	7.79	0.144	15.8
secondary NPH	7.8	7.7	0.906	-1.3	0.217	0.188	0.468	-13.4	6.1	6.6	0.792	8.2
age 50-	6.9	7.2	0.248	4.3	0.228	0.188	0.255	-17.5	6.3	6.2	0.937	-1.6
age 50+	8.1	7.9	0.688	-2.5	0.24	0.235	0.867	-2.1	6.6	8.3	0.099	25.8
all cases	7.5	7.5	0.89	0.0	0.234	0.212	0.326	-9.4	6.5	7.3	0.195	12.3

R resistance to outflow, *E* elastance, *P* the level of ICP

determine many parameters of CSF dynamics, of which outflow resistance (R) of CSF happens to be the most important [20]. However, in the case of non-shunted patients who are suspected of suffering from NPH there are only a few reports that have focused on repeated assessments of their hydrodynamic parameters as established by means of the LIT. The general view remains that the LIT is an examination that is consistently reliable [3, 11, 32–34]. In a small group of patients with hydrocephalus, the differences in R values in the follow-up as compared with those in the first assessment were found to be insignificant, i.e. not exceeding 5 % [3]. In the only large series of non-shunted NPH patients published to date [34] in which the LIT was repeated, significant correlations were found for the R, E, and the slope of the AMP-P line. The most inconsistent parameters found were the baseline ICP and the baseline pulse amplitude. Of all the parameters of the LIT, R had the best repeatability. Moreover, the authors concluded that the parameters must be considered within a range rather than as an absolute value. This is important, because

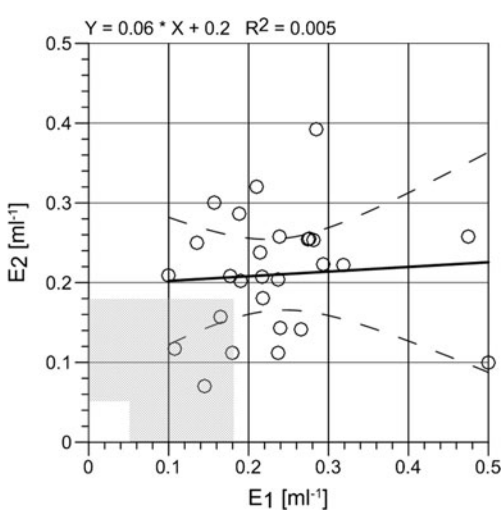

Fig. 2 The values of elastance in the first (E1) and the second (E2) assessment. The normal values of E (0.05 < E < 0.18) were marked (*shadow*)

there is no widely accepted threshold of R as far as its predictive value is concerned [17]. Investigations on healthy volunteers have shown that R does not exceed 10 mmHg/ml/min [1]. There is still no clear-cut borderline between physiological and pathological R: in many articles, the lowest level of R from which shunting is recommended varies from 8 to 13 mm/ml/min [2, 4, 13, 28, 31, 36, 41]. According to Boon et al. [5], the value of R is a reliable predictor of the outcome if the limit for shunting is raised to 18 mmHg/ml/min. At lower values of R, the decision depends mainly on clinical and CT results, which are typical for NPH. However, a recently published systematic review [17] has revealed that R value of 12 mmHg/ml/min is the most suitable threshold for predicting responsiveness in NPH patients, with a positive prediction of about 65 %.

LIT and CSF tapping are usually used together—as complementary tests—for the selection of NPH patients. The European Idiopathic NPH Multicentre Study [42] reports that the CSF tap test has an overall accuracy of 53 %, but adds that the combination of both tests does not improve their predictive power. False-negative predictions are much higher (58 %) in case of the tap test than in the case of the LIT (16 %) [16]. The tap test taken by itself has low sensitivity (26-61 %) [19]. Moreover, no correlation has been found between the R values and the results of CSF tapping [42]. We realized, that in our particular group of borderline NPH patients the assessment after CSF tapping could be doubtful because of their relatively good neurological condition (in all but three of them) and for this reason it was difficult to expect spectacular and unequivocal improvement as far as Hakim's triad was concerned. In this "less probable" NPH group, every adjunctive test is usually less likely to be positive as compared with the group of "shunt-responsive" cases. This evidence allows us to consider the tap test only as an additional factor which we expected to be helpful in the assessment of our group of cases. In fact, we were unable to confirm any positive role that was played by CSF tapping in these borderline cases. The parameters of the LIT did not change significantly in either assessment, despite the fact that the majority of presented cases had a decreased volume–pressure reserve. This was particularly true for R values, which were very stable (with mean values of 7.5 mmHg/ml/min). These results showed that there was no need to repeat the LIT, at least within the period of about 6 months following the first test. It is also important to remember that the LIT is an invasive technique that is associated with a certain risk of infection, local pain, and possible headache. For the patient, the LIT begins with the unpleasant experience of the lumbar puncture followed by a prolonged period of time spent in an uncomfortable lateral recumbent position.

Limitations

It is difficult to compare our group with other studies. Our series consisted of cases that had not been considered for shunting owing to their doubtful neurological signs, together with the negative tap test results. There were no cases that fulfilled the criteria for shunting and that did not agree to be operated. In our study, R and other hydrodynamic parameters were not taken as a first-line exclusive selection criteria. The mean value of R, however, was low (7.5 mmHg/ml/min.), which was an additional argument against shunting.

It has been well established in the literature that the hydrodynamic tests are usually considered to be helpful only in the selection of patients and not as a main criterion for shunting [5, 6, 12, 15, 17, 42]. However, an analysis of seven existing papers in which non-shunted cases were retrospectively or prospectively followed up revealed that in all but two of them it was arbitrarily defined hydrodynamic data decided which patients were to be shunted. Several hydrodynamic parameters have served as selection criteria for shunting, namely:

- the measurement of ICP [29] (a threshold of over 10 mmHg, or between 5 and 10 mmHg if A-waves are present in more than 30 % of the recorded time);
- ICP waves [9] (intracranial pulse pressure amplitudes in relation to different levels of ICP);
- the level of ICP, waves, and R [24] (a threshold basal pressure of over 10 mmHg + A and/or B waves in more than 10 % of the recorded time, and if not, the R value of more than10mmHg/ml/min);
- the LIT [6] (the R value and pulsatility during lumbar infusion);
- aqueductal stroke volume [30] (a threshold which is greater or equal to 42 ml).

In some of the above-mentioned groups of non-shunted cases that were analyzed, there were patients who refused surgical treatment, despite the fact that they fulfilled the neurological and hydrodynamic criteria for shunting [26, 30]. These patients should not be compared with those who did not qualify for shunting. Deterioration was obviously a likely outcome and indeed occur in some of the patients not long after the initial assessment. In our study, no patient deteriorated within the observation time and six cases (23 %) improved—mostly those with secondary NPH and those with no PVL, which might support the view that problems of CSF circulation were not responsible for their neurological signs. Exact assessment of all our non-shunted patients has been limited, however, because nine patients (out of a total of 36, i.e., 25 %) did not take part in the follow-up. Another factor that should be taken into consideration is that patients diagnosed with NPH are by no means a homogenous group. Mori and Mima [22] have reviewed studies on hydrocephalus and have concluded that in most cases of suspected NPH the primary causes are neurodegenerative changes (injury of the parenchyma usually caused by hemodynamic disturbances of vascular origin) and not cerebrospinal fluid resorption disorders. In developed hydrocephalus, both these factors coexist in various proportions. As a result, radiological and clinical presentations in these patients vary significantly. In our study, there were only a few patients who declared co-morbidities that might have influenced CSF resorption. These patients received appropriate treatment in order to reduce the potential influence of vascular co-morbidities on the value of R. It has been well established in the literature that in patients who have symptoms of NPH but in whom the value of R is normal, cerebrovascular pressure reactivity is disturbed, suggesting underlying CVD, which is more commonly found in these cases as compared with the group with an elevated R [8]. We did not directly analyze cerebrovascular reactivity by means of an assessment of the ICP waves in relation to the arterial blood pressure.

NPH is a chronic disease, and the exact time for the follow-up of these patients has yet to be established. Our arbitrarily assumed time of nearly 6 months for the second assessment should therefore be established by another follow-up in order to gain a more comprehensive knowledge of the natural course of the disorder in non-shunted NPH cases.

Only a prospective randomized multicenter study of a group that is as homogenous as possible can provide credible evidence [40].

Conclusions

1. Patients suspected of having NPH in whom there are no convincing criteria for CSF diversion should not be qualified for shunting because we can expect that they will not deteriorate and some of them may even significantly improve as far as the level of dementia is concerned. The time limit for further assessment, however, remains unclear.
2. Given that controlled CT scans, as well as the parameters of a LIT performed a second time, are stable, there would seem to be no need for them to be repeated, at least within

the period of nearly six months after the primary diagnosis.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Statement of the human rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Statement on the welfare of animals This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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Comments

This is an interesting study on borderline NPH patients who did not qualify for shunting and were retested regarding clinical parameters and objective lumbar infusion test results. It could be shown that short-term prognosis is good without neurosurgical treatment. The object of this series is well chosen and methodology is adequate. Only a few questions should possibly be discussed in addition: Is it possible that initial CSF tapping can play a positive role in these borderline cases? Did the patients present with comorbidities that potentially may influence CSF resorption at any time (e.g., heart or vascular diseases)? If yes, had they appropriate treatment and remained stable accordingly? Is it useful to have another clinical follow-up after a longer interval compared to the 5.6 months?

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