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EDITORIAL

Post-traumatic hydrocephalus: the Cinderella of Neurotrauma

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1. Introduction

Traumatic brain injury still represents one of the leading causes of death and disability, with 50 million new cases each year worldwide and mortality rates as high as 30–40% [1].

Post-traumatic hydrocephalus may develop weeks to months after brain injury. Its incidence deeply varies among series (0.7–50%), and this is mainly due to very different diagnostic criteria [2].

Therefore, given the very high number of patients with traumatic brain injury, patients presenting with post-traumatic hydrocephalus are not infrequent.

Nonetheless, post-traumatic hydrocephalus probably represents the 'Cinderella without fairy-godmother' of Neurotrauma. In fact, while these patients are daily encountered in Neurology, Neurosurgery and Rehabilitation Departments, Pubmed search only retrieves less than 100 published papers on this topic (search terms: 'post-traumatic hydrocephalus' OR 'post-traumatic ventriculomegaly': 86 papers on 15 April 2020). Most of these papers are on natural history or predictive factors [3,4].

Very few studies deal with diagnosis, treatment modalities and criteria to identify treatment responders [5–8].

In this context, the Cambridge group has recently published a very interesting paper on CSF dynamics analysis of patients with post-traumatic ventriculomegaly [9]. The choice of the term ventriculomegaly in the title reflects the difficulty in differentiating a ventricular enlargement (secondary to post-traumatic brain damage with atrophy) from an active, hydrocephalic process.

The authors are to be congratulated, since the topic is certainly of interest and deserves to be better studied. As an example, in a recent review on post-traumatic hydrocephalus, CSF dynamic studies are not even cited as a possible diagnostic tools (https://emedicine.medscape.com/article/326411-overview).

2. Methods and results

In their paper, the authors retrospectively analyzed the infusion tests performed on 36 patients with post-traumatic ventriculomegaly [9]. They calculated the resistance to CSF outflow (Rout), AMP (pulse amplitude of intracranial pressure, ICP), dAMP (AMPplateau-AMPbaseline). Sixteen out of 36 patients were selected for surgery (ventriculoperitoneal shunt), based on consultant judgment. Only 5 out of 16 patients improved after shunting. These patients seemed to have higher Rout values, and this was consistent with the higher Rout values the authors found in their 'control' group, that was made of shunt responders patients with normal pressure hydrocephalus. Mean Rout in post-traumatic ventriculomegaly patients (36 cases) was lower than Rout of normal pressure hydrocephalus shunt-responders (13.53 ± 5.21 vs 19 ± 8.91). Particularly, mean Rout in patients with post-traumatic ventriculomegaly was: 13.53 ± 5.21 (all 36 cases), 16.73 ± 5.67 (shunted patients-16 cases), 18.86 ± 5.13 (shunt responders: 5 out of 16 shunted patients).

3. Discussion

The first paper suggesting to differentiate post-traumatic ventriculomegaly from post-traumatic hydrocephalus using opening intracranial pressure and infusion test was written by Marmarou in 1996 [5]. Nonetheless, in that paper the authors analyzed the natural history of intracranial pressure and outflow resistance in patients with post-traumatic ventriculomegaly, but did not identify criteria for surgery and shunt responsiveness.

Lalou et al [9] incorrectly wrote that 'To best knowledge, other infusion test parameters besides ICP and Rout have not been studied in PTH … The fact that there is no high-grade evidence for using infusion tests for patients with PTH was one reason for us to study the subject, since no one has attempted to build the evidence since Marmarou'.

In fact, almost 20 years after Marmarou, De Bonis et al [6] published the first paper on CSF analysis in patients with post-traumatic hydrocephalus and tried to understand if a combination of infusion test parameters (opening pressure, outflow resistance and intracranial elastance index) could help identifying shunt responders [6]. The intracranial elastance index was calculated as the slope of the linear regression between diastolic ICP (dICP) and the corresponding pulse amplitude (pulse pressure) per each wave [6,10]. The main advantage of that paper was that all patients underwent surgery. De Bonis et al [6] found that higher R-out (cutoff >10 mmHg/ml/min) had 100% sensitivity, 50%

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Article highlights

- Post-traumatic hydrocephalus is not infrequent, but pathophysiology, diagnostic criteria, identification of treatment responders and treatment modalities remain unclear
- Very few papers have been published on this topic, and most of these papers deal with risk factors and natural history
- Lalou et al. published a paper on CSF dynamics analysis in patients with post-traumatic ventriculomegaly, showing these patients present a mean lower CSF outflow resistance compared with patients with normal pressure hydrocephalus that responded to shunt surgery
- Similarly, other studies tried to differentiate ventriculomegaly from an active hydrocephalus with CSF dynamics analysis, analyzing opening pressure, CSF outflow resistance and intracranial elastance.
- Patients with post-traumatic hydrocephalus who respond to surgery probably have a higher CSF outflow resistance, but this parameter alone is not sufficient to indicate or rule out surgery.
- Other studies are needed, since while patients are frequent, this topic seems to be of little interest, and therefore post-traumatic hydrocephalus remains an unfortunate Cinderella without a fairy-godmother.

specificity, 100% negative predictive value and 63.6% positive predictive value. Elastance index (cutoff value >0.3) had 100% specificity, 42.4% sensitivity, 66.7% negative predictive value and 100% positive predictive value. Therefore, a combination of Intracranial Elastance and of R-out could help predicting shunt responsiveness.

Finally, in 2017 also some indian authors measured opening pressure, pressure-volume index and Rout and compared patients with normal pressure hydrocephalus and patients with post-traumatic hydrocephalus [8]. Following Marmarou flowchart, they shunted patients with high pressure hydrocephalus and with elevated Rout (3 cases out of 8): all these patients improved.

Another very difficult element to consider for this disease is patient selection.

In fact, practically all patients with post-traumatic ventricular enlargement present with symptoms of post-traumatic lesions and almost never present with the Hakim-Adams triad [2,6]. Some of them present nonspecific symptoms, especially arrested clinical improvement during rehabilitation programs, impaired consciousness or a worsening neurologic status [2]. These conditions lead the clinicians to perform further brain CT-MRIs eventually showing a ventricular enlargement. Here is the reason why De Bonis et al [6]. only selected patients using radiological criteria and all patients underwent CSF shunt. In Lalou series [9], instead, selection of patients for surgery varied and included several non-standardized factors. This cannot allow a precise estimate of positive and negative predictive values of infusion test parameters.

Curiously, Lalou et al [9] included patients whose time interval between the TBI and infusion varied from 10 days to 33.5 years. How can post-traumatic hydrocephalus develop or be cured 33 years after trauma remains unclear.

Other aspects that needed to be better explained and discussed were the lack of clinical criteria to establish shunt responsiveness: we do not know pre-operative symptoms, therefore 'documentation of improved symptoms at 6 months' should have been better specified [9].

Moreover, they performed infusion tests either under local or under general anesthesia [9]. The infusion test parameters are deeply influenced by general anesthesia, since general anesthesia alters (and controls) respiration, systemic arterial pressure (and consequently intracranial pressure) and venous pressures [11].

Finally, the statements on external hydrocephalus 'due to impairment of CSF absorption in Pacchionian granulations' refer to old theories. More recently, it has been postulated that external hydrocephalus may initially derive from a lacerated arachnoid and often precedes hydrocephalus for an impairment of intracranial venous outflow or alteration of the glymphatic system [12–14].

Similarly, recent papers have postulated a possible role of inflammation and high fibrosis in the pathogenic mechanism of PTH [15,16].

We do perfectly agree with the authors that there are no guidelines specifying criteria for performing infusion tests in TBI patients and therefore practice amongst consultants could have been variable.

We also agree that infusion tests should be performed only in non-decompressed patients. If decompressive craniectomy had been previously performed, a cranioplasty should have been performed 4 weeks or more before the infusion to allow for restoration of the intracranial system (CSF as well as cerebral blood flow) [17,18].

In this series, Lalou [9] observed that 5 out of 16 shunted patients improved and these patients presented higher Rout values. Three out of 16 patients presented complications. Also Ramesh [8] and De Bonis [6] noticed that high Rout values (cutoff not identifiable due to slightly different infusion methods) have a very high sensitivity of shunt response. Unfortunately, shunt procedure risks in these patients are not negligible. Therefore, we encourage researchers to study these patients, to share and compare their data, in order to obtain significant results for better selecting patients for surgery.

4. Five-year view

In the years to come, patients with brain injury are going to decrease, due to an improvement of technologies aimed to protect the head during motor-vehicle accidents and at work. Nonetheless, this number will continue to be very high. Therefore, the number of patients with post-traumatic hydrocephalus is expected to slightly decrease.

Research groups, especially young researchers, should be encouraged to help understanding the pathophysiology of this disease. Studying the intracranial system is not simple, since it implies knowledge of physics (hydraulic and gravity forces) as well as human physiology. To date, the most fruitful research groups on this topic have created a multidisciplinary team of Engineers, Physics, Biologists and Neurosurgeons. This will be one of the winning keys. Mathematical and Physical models of physiological and altered intracranial system are needed, mimicking pathological entities. If pathophysiological mechanisms will be known, therefore therapy will follow.

Future directions will probably be constituted by novel imaging studies (molecular imaging, dynamic molecular imaging), aimed at directly visualizing on-site molecules movements and concentrations over time, cell volume, cell-to-cell

interactions, whole intracranial system fluids movements (intraparenchymal and extraparenchymal). Currently available MRI technologies are too raw for these aims and often derive from mathematical algorithms based on an approximate, often incorrect knowledge of physiology.

If the new generations of Biologists, Doctors, Engineers, Physicists and Mathematicians will fall in love with this topic nobody wants to deal with, they will probably act as the fairy godmother and change the fate of Cinderella/post-traumatic hydrocephalus.

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References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Majdan M, Plancikova D, Brazinova A, et al. Epidemiology of traumatic brain injuries in Europe: a cross-sectional analysis. Lancet Public Health. 2016 Dec;1(2):e76–e83.
2. Mazzini L, Campini R, Angelino E, et al. Posttraumatic hydrocephalus: a clinical, neuroradiologic, and neuropsychologic assessment of long-term outcome. Arch Phys Med Rehabil. 2003 Nov;84 (11):1637–1641.
   •• ***This is a clear paper on symptoms, signs, diagnostic criteria and tools of patients with post-traumatic hydrocephalus.***
3. Nasi D, Gladi M, Di Rienzo A, et al. Risk factors for post-traumatic hydrocephalus following decompressive craniectomy. Acta Neurochir (Wien). 2018 Sep;160(9):1691–1698.
4. De Bonis P, Pompucci A, Mangiola A, et al. Post-traumatic hydrocephalus after decompressive craniectomy: an underestimated risk factor. J Neurotrauma. 2010 Nov;27(11):1965–1970.
5. Marmarou A, Foda MA, Bandoh K, et al. Posttraumatic ventriculomegaly: hydrocephalus or atrophy? A new approach for diagnosis using CSF dynamics. J Neurosurg. 1996 Dec;85(6):1026–1035.
   •• ***This is the first paper proposing to study patients with post-traumatic ventriculomegaly with CSF dynamics analysis. Unfortunately, they did not present a case series.***
6. De Bonis P, Mangiola A, Pompucci A, et al. CSF dynamics analysis in patients with post-traumatic ventriculomegaly. Clin Neurol Neurosurg. 2013 Jan;115(1):49–53.
   • ***This is the first paper analysing CSF dynamics in a series of patients with post—traumatic ventriculomegaly.***
7. De Bonis P, Tamburrini G, Mangiola A, et al. Post-traumatic hydrocephalus is a contraindication for endoscopic third-ventriculostomy : isn't it? Clin Neurol Neurosurg. 2013 Jan;115(1):9–12.
8. Ramesh VG, Narasimhan V, Balasubramanian C. Cerebrospinal fluid dynamics study in communicating hydrocephalus. Asian J Neurosurg. 2017 Apr-Jun;12(2):153–158.
9. Lalou AD, Levrini V, Czosnyka M, et al. Cerebrospinal fluid dynamics in non-acute post-traumatic ventriculomegaly. Fluids Barriers CNS. 2020 Mar 30;17(1):24.
10. Anile C, De Bonis P, Albanese A, et al. Selection of patients with idiopathic normal-pressure hydrocephalus for shunt placement: a single-institution experience. J Neurosurg. 2010 Jul;113 (1):64–73.
11. Eide PK, Due-Tønnessen B, Helseth E, et al. Assessment of intracranial pressure volume relationships in childhood: the lumbar infusion test versus intracranial pressure monitoring. Childs Nerv Syst. 2001 Jun;17(7):382–390.
12. Eide PK, Valnes LM, Pripp AH, et al. Delayed clearance of cerebrospinal fluid tracer from choroid plexus in idiopathic normal pressure hydrocephalus. J Cereb Blood Flow Metab. 2019 Sep 7. [Epub ahead of print]. DOI:10.1177/0271678X19874790
13. Mantovani G, Menegatti M, Scerrati A, et al. Controversies and misconceptions related to cerebrospinal fluid circulation: a review of the literature from the historical Pioneers' theories to current models. Biomed Res Int. 2018 Nov 26;2018:2928378.
   • ***In this paper, the authors show that several experiments have denied classical theories on CSF circulation.***
14. De Bonis P, Sturiale CL, Anile C, et al. Decompressive craniectomy, interhemispheric hygroma and hydrocephalus: a timeline of events? Clin Neurol Neurosurg. 2013 Aug;115(8):1308–1312.
15. Karimy JK, Reeves BC, Damisah E, et al. Inflammation in acquired hydrocephalus: pathogenic mechanisms and therapeutic targets. Nat Rev Neurol. 2020;16:285–296.
16. Hao X, Junwen W, Jiaqing L, et al. High fibrosis indices in cerebrospinal fluid of patients with shunt-dependent post-traumatic chronic hydrocephalus. Transl Neurosci. 2016 Sep 9;7(1):92-97.
17. Czosnyka M, Copeman J, Czosnyka Z, et al. Post-traumatic hydrocephalus: influence of craniectomy on the CSF circulation. J Neurol Neurosurg Psychiatry. 2000 Feb;68(2):246–248.
18. Waziri A, Fusco D, Mayer SA, et al. Postoperative hydrocephalus in patients undergoing decompressive hemicraniectomy for ischemic or hemorrhagic stroke. Neurosurgery. 2007 Sep;61 (3):489–493.
   • ***In this paper, the author showed that early cranioplasty could restore normal CSF dynamics.***