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Successful treatment of negative pressure hydrocephalus using timely titrated external ventricular drainage: a case series☆

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ABSTRACT

Objective: Negative-pressure hydrocephalus (NegPH) is a rare clinical entity characterised by enlarged ventricles and symptoms consistent with increased intracranial pressure (ICP) in the setting of negative ICP. Little has been published regarding appropriate treatment and outcomes of negative-pressure hydrocephalus patients, and no data have been published demonstrating successful therapy producing acceptable long-term outcomes. Here we present 8 cases successfully treated by titrated external ventricular drainage (TEVD), including drainage at negative (subatmospheric) pressure, and subsequent low-pressure ventriculoperitoneal shunting.

Methods: A retrospective audit of all cases of negative-pressure hydrocephalus occurring at a university teaching hospital between 2006 and 2012 was undertaken. The clinical features of these cases, results of radiological investigations, treatment, and outcome were drawn from the patients' records.

Results: Eight cases of NegPH were identified. All patients had at least one preceding intracranial procedure (mean number of procedures 3.0). All cases were treated using TEVD, titrated to produce between 5 and 15 mL per hour of CSF drainage, including drainage under subatmospheric pressure if this was required to maintain CSF flow. Mean delay from first negative ICP to TEVD was 1.8 days. All 8 patients demonstrated clinical improvement. TEVD resulted in improvement in Glasgow Coma Scale (mean increase 4.6, $p = 0.003$), and increases in ICP (mean increase 8.5, $p < 0.001$). Mean length of follow-up was 471.8 days. At follow-up, four patients had returned to pre-morbid functioning, three had a reduction in functioning attributable to their initial presentation (not NegPH), and one had died of unknown cause. Illustrative case descriptions are included.

Conclusions: Negative-pressure hydrocephalus is a rare but underrecognised syndrome that can be successfully treated by timely external ventricular drainage titrated to maintain CSF flow, and subsequent low-pressure ventriculoperitoneal shunting.

1. Introduction

Negative-pressure hydrocephalus (NegPH) is a rare condition that is characterised by enlarged ventricles and symptoms consistent with increased intracranial pressure in the setting of negative intracranial pressure (ICP). The first description of NegPH was provided by Vassilyadi et al., who reported 2 paediatric patients with hydrocephalic symptoms, negative ICP, and clinical improvement with modification of cystopleural shunts to increase flow resistance [1]. Since this initial report, a total of five further cases have been reported in the literature, by Clarke and her colleagues, and Fillipidis et al. [2,3]. In 2006, Clarke et al. described two cases of likely NegPH treated with negative-pressure drainage of cerebrospinal fluid (CSF) and clinical response that was initially promising. Unfortunately, ultimate clinical outcome in both cases was poor; both patients were non-verbal at follow-up, one was bedridden and the other had been admitted to a residential care facility [2]. Notable in this series was a prolonged time from initial symptoms to ultimate treatment with external ventricular drainage. In 2011, Fillipidis et al. described a further 3 patients with low or negative-pressure hydrocephalus following surgical approaches to the cranial base [3]. Two of these patients improved with repair of CSF leaks and external ventricular drainage that was titrated to produce CSF

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flow; both of these cases required drainage under subatmospheric pressures. Ultimately, one of these patients was provided with a ventriculoperitoneal shunt (VPS), and one was palliated due to poor progress. Their third case demonstrated clinical improvement solely with repair of a frontal CSF leak. In this paper we present the first series describing statistically significant clinical, manometric, and radiological improvement following treatment for NegPH, with data on long-term patient outcomes.

2. Materials and methods

A retrospective audit of all neurosurgical cases occurring between 2006 and 2012 at a university teaching hospital was undertaken to identify cases of NegPH. Cases were drawn from the neurosurgical patient database. Cases were included if (i) a negative ICP was measured, (ii) there was concurrent radiographic evidence of ventriculomegaly, (iii) the patient was suffering symptoms that were attributable to hydrocephalus and coincided temporally with negative ICP and ventriculomegaly, and (iv) malfunction of the ICP monitor and other equipment had been excluded. ICP was monitored using strain gauge tipped intracranial catheters manufactured by Codman (Raynham, Massachusetts, USA), or via an external ventricular drain (EVD) (in all cases manufactured by Medtronic, Minneapolis, Minnesota, USA). EVDs were levelled to the tragus at the beginning of each nursing shift. Clinical parameters were monitored by trained neurosurgical nurses in a neurosurgical high dependency unit. Computed tomography (CT) scans were performed using a Siemens Somatom Definition AS scanner (Erlangen, Germany).

Data was gathered on patients' clinical parameters, including previous procedures, longitudinal data on ICPs, conscious state, treatment of NegPH, and outcome data. Statistical tests were performed using GraphPad Prism 6 (Graphpad Software, California, USA). Two-tailed paired *t*-tests were performed for continuous variables measured on each patient. A P value of less than 0.05 was used to determine significance.

3. Results

Eight patients met the inclusion criteria, and relevant clinical details are summarised in Table 1. 5 were males. The teaching hospital from which these cases arose has a well-defined catchment population, which enabled estimation of the incidence of NegPH at 1 case per 380 250 people per year. The mean age at development of NegPH was 47.3 years (range 12–70 years, standard deviation (SD): 20.4 years). All patients had at least 1 preceding neurosurgical procedure, with the mean number of procedures 3.0 per patient (range 1–7, SD: 2.0).

All patients were treated by external ventricular drainage that was titrated to maintain CSF flow volumes of between 5 and 15 mL per hour (titrated external ventricular drainage, TEVD), depending on clinical progress. This included negative-pressure drainage if this was required to maintain CSF flow. Negative-pressure drainage was required in 6 cases. The mean time from first measured negative ICP to commencement of TEVD was 1.8 days (range 0–8 days, SD: 2.7 days). The mean duration of TEVD was 3.2 days (range 1–5 days, SD: 1.5 days). ICP prior to TEVD averaged −3.1 centimetres of water (cmH_2O) (range −1 to −7 cmH_2O, SD: 1.9 cmH_2O). Lowest recorded ICP averaged −6.5 cmH_2O (range −3 to −14 cmH_2O, SD: 1.9 cmH_2O). Average ICP following TEVD was 5.0 cmH_2O (range 2–7 cmH_2O, SD 1.9). The difference between ICP before and after TEVD was significantly different (mean increase 8.5 cmH_2O, $p < 0.001$). Mean GCS prior to TEVD was 9.4 (range 5–14, SD: 2.9). Following TEVD mean Glascow Coma Scale (GCS) was 14

Table 1
Characteristics of negative-pressure hydrocephalus patients.

Case number	Age (y)	Sex	Primary disease process	Definitive therapy	Length of follow-up (days)	Alive/dead	Functional outcome
1	27	M	Pineal germinoma	VPS with Medtronic Strata II valve set at 0.5	1538	Alive	Returned to work and premorbid function
2	51	M	Tectal plate cavernoma	VPS with Medtronic Strata NSC valve set at 0.5	806	Alive	CN VI palsy, balance difficulty
3	65	F	Metastatic adenocarcinoma of unknown origin	VPS with Medtronic Strata NSC valve set at 0.5	700	Alive	Undergoing chemotherapy, balance difficulty
4	12	M	Severe traumatic brain injury	VPS with Medtronic Strata II valve set at 1.0	345	Alive	Attending school with teaching aides
5	36	M	Severe traumatic brain injury	VPS with Medtronic Strata NSC valve set at 0.5	200	Alive	Returned to premorbid function, mobilising with support
6	54	F	Aneurysmal subarachnoid haemorrhage	VPS with Medtronic Strata NSC valve set at 0.5	100	Alive	Returned to work and premorbid function
7	70	F	Left MCA aneurysm, elective clipping	VPS with Medtronic Strata NSC valve set at 0.5	48	Dead	Discharged to an external hospital, died of unknown cause 48 days later
8	63	M	Aneurysmal subarachnoid haemorrhage	VPS with Medtronic Strata NSC valve set at 0.5	37	Alive	Returned to work and premorbid function

EVD, external ventricular drain; MCA, middle cerebral artery; VPS, ventriculoperitoneal shunt.