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Continuous Epidural Infusion of Hydroxyethyl Starch for Spontaneous Intracranial Hypotension: A Retrospective Case Series

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Case series
Patients: Female, 36-year-old • Male, 45-year-old • Female, 35-year-old • Male, 35-year-old
Final Diagnosis: Spontaneous intracranial hypotension
Symptoms: Headache
Clinical Procedure: —
Specialty: Anesthesiology • Neurology • Neurosurgery
Objective: Rare disease

Background: Spontaneous intracranial hypotension is a challenging clinical entity, conventionally managed through epidural blood patching. In a subset of refractory patients who have exhausted all standard-of-care therapies, suboptimal response or recurrence are major clinical concerns and can lead to prolonged symptoms, repeated interventions, and a heavier healthcare burden. Therefore, we describe an innovative intervention—continuous epidural infusion of hydroxyethyl starch—for the treatment of spontaneous intracranial hypotension, which is intended to provide sustained modulation of epidural pressure and to potentially promote closure of cerebrospinal fluid leaks.

Case Reports: This retrospective case series included 4 individuals diagnosed with spontaneous intracranial hypotension, all with orthostatic headaches. Three had non-traumatic subdural hematomas, among whom 2 underwent hematoma evacuation along with intracranial pressure monitoring within the subdural space. In contrast to conventional management strategies, these patients were treated with continuous epidural infusion of hydroxyethyl starch via epidural catheterization, with infusion parameters titrated to clinical response and, when available, intracranial pressure measurements. All patients had favorable clinical outcomes, with marked symptom relief, functional recovery, and no recurrence during follow-up. No major neurological complications or rebound intracranial hypertension occurred.

Conclusions: The patients' responses to continuous epidural infusion of hydroxyethyl starch were uniformly positive, offering a promising outlook for the treatment of spontaneous intracranial hypotension. Larger prospective studies are needed to confirm its safety and efficacy.

Keywords: Spontaneous Intracranial Hypotension • Headache • Subdural Hematoma • Epidural Blood Patching • Continuous Epidural Infusion of Hydroxyethyl Starch
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Introduction

Spontaneous intracranial hypotension (SIH) is a perplexing manifestation characterized by the unexpected leakage of cerebrospinal fluid (CSF) within the spinal canal [1]. Among its spectrum of complications, subdural hematoma (SDH) has come to the forefront as a significant concern. The association between SDH and SIH was initially documented in the 1950s [2]. The incidence of SDH in the context of SIH has been reported to range from approximately 15% to 35% in previous studies [3,4]. SIH can be treated variously, using conservative strategies like bed rest and hydration, along with percutaneous epidural patching and a range of surgical or endovascular interventions aimed at rectifying CSF leaks or fistulas [1]. While most SIH cases exhibit promising responses to conventional epidural blood patching (EBP), some require repeated applications [5,6]. While complications stemming from EBP are relatively rare, they remain an ever-present threat [7]. Notably, the propensity for CSF leakage relapse continues to challenge clinicians [8]. Moreover, the quandary deepens in instances where symptomatic SDH due to SIH assumes a critical clinical profile, demanding prudent SDH evacuation [4,9]. Within this complex therapeutic milieu, saline and hydroxyethyl starch (HES) have also been employed as alternatives to autologous epidural blood injection for the treatment of SIH [10,11]. Epidural saline patches have demonstrated inferior long-term efficacy compared with EBP in the treatment of post-dural puncture headache (PDPH) [12]. Continuous epidural saline infusion has shown moderate efficacy in the management of SIH; however, its therapeutic benefit is generally transient, depends on uninterrupted administration, and often requires prolonged treatment durations [10]. In contrast, owing to its greater viscosity and higher molecular weight, HES can persist longer within the epidural space and provide a more sustained effect [13]. Consistent with this rationale, previous reports have described epidural injection of HES as a viable therapeutic option for CSF-cutaneous fistula, PDPH, and SIH [11,13,14]. However, experimental evidence indicates that the increase in epidural pressure following a single HES injection is short-lived [15], providing the rationale for the development of continuous epidural infusion of HES for PDPH prevention [13]. Collectively, these observations support an emerging paradigm shift toward continuous epidural infusion of HES as a potentially innovative therapeutic strategy.

Against this backdrop, we embarked on a therapeutic journey centered around continuous epidural infusion of HES, steering away from the conventional and aiming to illuminate a novel path in the management of SIH.

Case Reports

Case 1

A 36-year-old woman presented to our neurology department due to orthostatic headaches for 4 days. Brain magnetic resonance imaging (MRI) revealed pachymeningeal enhancement (**Figure 1A**) and bilateral subdural effusions (**Figure 1B**). The patient was diagnosed with SIH and received conservative management upon her hospitalization. On hospital day 12, she developed blurred vision and unequal pupils. These new symptoms prompted an EBP procedure at the L2-L3 level on day 14, which resulted in a notable improvement in the headache and resolution of the ocular symptoms. Subsequent brain computed tomography (CT) scan conducted on day 21 revealed bilateral frontoparietal and temporal SDHs, predominantly on the right (**Figure 1C**). Persistent headaches accompanied this finding. Consequently, on day 24, she underwent right-sided SDH drilling and drainage procedures and subdural intracranial pressure (ICP) monitoring. Continuous ICP monitoring was performed using a Sophia PSO-3000 system after surgery, with ICP values recorded hourly, while the patient was positioned supine in a quiet environment. Postoperatively, her headache symptoms improved, and bilateral subdural effusions and hemorrhage decreased (**Figure 1D**), although ICP monitoring continued to show low ICP. On day 25, continuous epidural infusion of HES was initiated at the L2-L3 level following aseptic epidural catheter placement (catheter depth: 15 cm). The infusion involved the slow injection of 20 mL of 6% HES 130/0.4 (Voluven®, Fresenius Kabi, China) into the epidural space through the epidural catheter, followed by continuous infusion via a patient-controlled epidural analgesia device filled with HES. Infusion rates were regulated, with adjustments made according to symptoms and ICP dynamics. The patient was instructed to stay in bed during the first few days, but could roll over and move her limbs to prevent thrombosis. The epidural HES infusion was discontinued on day 30, after which she was instructed to gradually resume normal activities of daily living. She reported no headaches at discharge and at follow-ups after discharge. Subsequent brain CT scans at discharge (**Figure 1E**) and 1 month after discharge (**Figure 1F**) showed no hematoma recurrence. Additional details are presented in **Tables 1 and 2**.

Case 2

A 45-year-old man presented to our neurosurgery department due to a 2-month history of orthostatic headache. An initial brain CT scan revealed bilateral frontoparietal and temporal SDHs (**Figure 2A**). Following admission, the patient reported an exacerbation of headache despite pharmacological treatment. On hospital day 4, surgical intervention was deemed necessary, and bilateral SDH evacuation was performed. A postoperative brain CT scan showed epidural and subdural collections,

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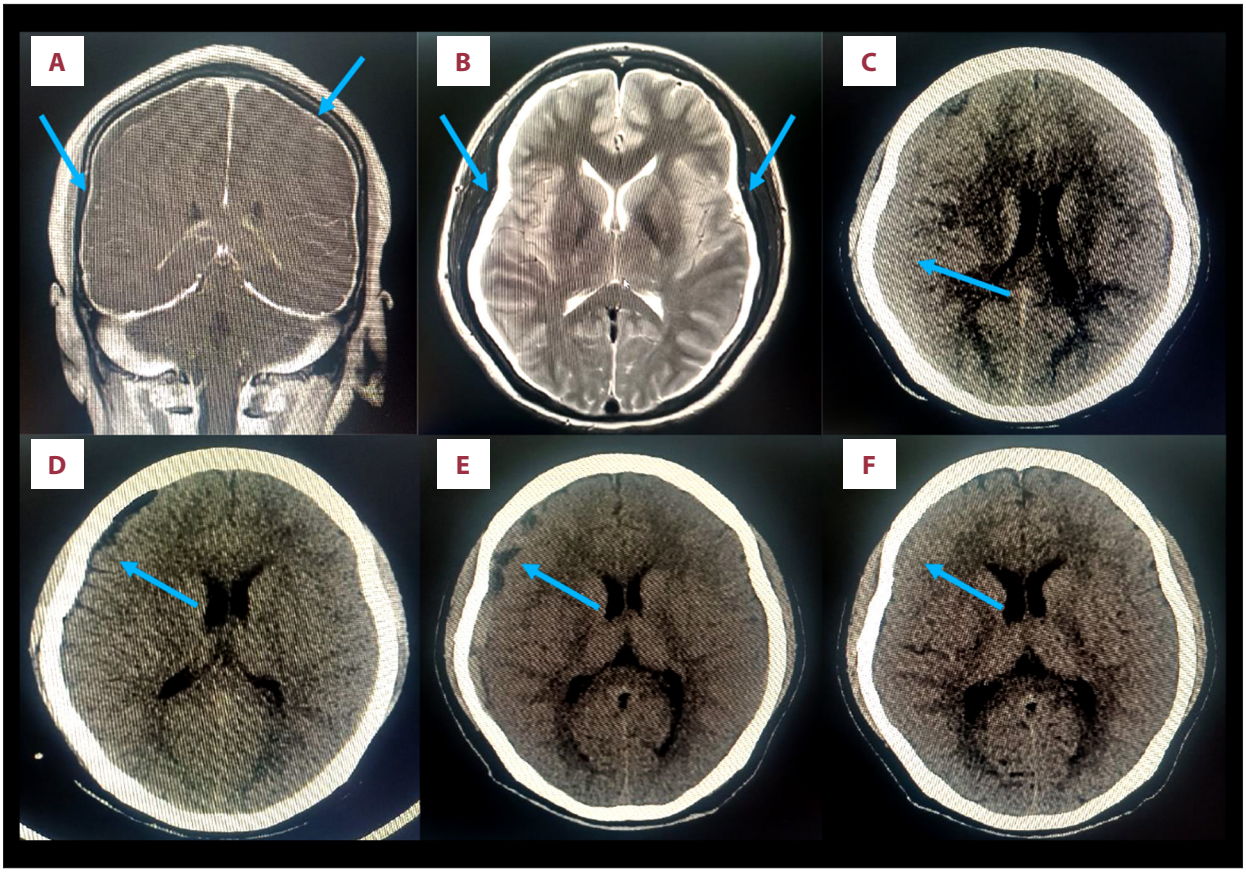

Figure 1. (**A**) Brain T1 gadolinium-enhanced MRI demonstrating diffuse, continuous, linear enhancement of pachymeninges (blue arrow). (**B**) Brain T2-weighted MRI revealing bilateral subdural effusions (blue arrow). (**C**) Preoperative brain CT illustrating bilateral frontoparietal and temporal chronic SDHs, predominantly on the right side (blue arrow, maximum thickness of SDH: 11 mm). (**D**) Brain CT on postoperative day 2 following burr-hole drainage of bilateral frontoparietal and temporal SDHs, indicating an improvement of bilateral frontoparietal and temporal subdural effusions and hemorrhage compared with those in the anterior regions (blue arrow). (**E**) Brain CT at discharge showing no evidence of hematoma recurrence (blue arrow). (**F**) Brain CT conducted 1 month after discharge displaying no hematoma recurrence (blue arrow).

predominantly in the left frontoparietal region (**Figure 2B**). On the same night as the initial surgical intervention, the patient underwent a secondary procedure involving drilling and drainage of the epidural hematoma, concomitant with ICP probe insertion. Postoperatively, both the headache and the epidural and subdural collections improved (**Figure 2C**). Continuous ICP monitoring indicated low cranial pressure, raising suspicion for SIH. On day 5, continuous epidural infusion of HES was initiated following catheterization at the L2–L3 level (catheter depth: 18 cm), using the same infusion protocol and precautions as in Case 1. On day 4 of epidural HES infusion, the epidural catheter was accidentally dislodged and subsequently repositioned at the L1-L2 (catheter depth: 18 cm). The infusion ceased on day 12, and the patient was instructed to gradually resume normal daily activities. He reported no recurrence of headache at discharge or during follow-up. No new hematoma was detected on brain CT at discharge (**Figure 2D**). Further details are presented in **Tables 1 and 2**.

Case 3

A 35-year-old woman was transferred to our neurology department due to a 1-month history of orthostatic headache. Brain MRI unveiled bilateral subdural effusions, swelling of the superior pituitary margin, and extensive meningeal enhancement. She was diagnosed with SIH and underwent an EBP procedure at the referring hospital. A subsequent MRI scan revealed bilateral frontoparietal and temporal SDHs, with persistent headache, prompting transfer to our hospital for further treatment. On hospital day 3, continuous epidural infusion of HES was initiated following catheterization at the L3-L4 level (catheter depth: 15 cm). The infusion protocol, including all precautions, was identical to that used in Case 1, although the infusion rate was adjusted according to the patient's evolving symptoms. Epidural HES infusion was discontinued on day 8, and the patient was instructed to gradually resume normal daily activities. A subsequent CT scan unveiled bilateral frontoparietal and

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Table 1. Clinical characteristics and disease progression.

Case	Case 1	Case 2	Case 3	Case 4
Sex/age	F/36 years	M/45 years	F/35 years	M/35 years
Description of orthostatic headache	A sharp or stabbing pain in the parietal-occipital region	Severe, bilateral frontotemporal headache	Generalized head pain with a sensation of swelling	Occipital headache triggered by air travel
Associated symptoms	Nausea	Dizziness and cerebral distension	Dizziness, tinnitus, and non-jet vomiting	Nausea and vomiting
History of major trauma and lumbar puncture	None	None	None	None
Significant prior medical history	None	Asthma	None	None
Neurological examination	Normal	Normal	Normal	Normal
Treatment approaches	Conservative treatment EBP SDH evacuation Epidural HES infusion (administered on hospital days 25 to 30)	Pharmacological therapy SDH evacuation Epidural hematoma evacuation Epidural HES infusion (administered on hospital days 5 to 12)	EBP Epidural HES infusion (administered on hospital days 3 to 8)	Conservative treatment Epidural HES infusion (administered on hospital days 9 to 12)
Headache status when sitting	None (hospital day 28)	None (hospital day 10)	None (hospital day 7)	None (hospital day 16)
Headache status when walking slowly	None (hospital day 29)	None (hospital day 11)	None (hospital day 8)	Slight headache (hospital day 17)
Headache status at discharge	None (hospital day 43)	None (hospital day 19)	None (hospital day 14)	Slight headache (hospital day 17)
Telephone follow-up	No headache attacks at months 6, 12, and 48 after discharge	No headache attacks at months 6, 12, and 29 after discharge	No headache attacks at months 6, 12, and 48 after discharge	No headache attacks at months 6, 12, and 47 after discharge

Abbreviations: EBP, epidural blood patching; SDH, subdural hematoma; HES, hydroxyethyl starch; F, female; M, male.

temporal subdural effusions (**Figure 3**). The patient reported no headache at discharge on day 14 or during post-discharge follow-ups. Further details are illustrated in **Tables 1 and 2**.

Case 4

A 35-year-old man presented to our neurology department due to a 1-month history of orthostatic headache. Brain MRI revealed bilateral subdural effusions (**Figure 4A**), mild elevation of the superior pituitary margin (**Figure 4B**), and subtle dilation of the venous sinuses (**Figure 4C**). A diagnosis of SIH was established, and conservative therapy was initiated on admission; however, the clinical response was suboptimal. On hospital day 9, continuous epidural infusion of HES was initiated following catheterization at the L2-L3 level (catheter depth: 12 cm), using the same infusion protocol and precautions as in Case 3. On day 12, the epidural catheter was removed due to intolerable left lumbar and hip pain, and the patient was instructed to gradually resume normal daily activities. By day 17, he had a very slight headache during ambulation and was discharged with no lumbar or hip discomfort. After discharge, he achieved complete resolution of headache following an additional week of intravenous fluid therapy administered at another medical facility. During the post-discharge follow-up period, he remained free of recurrent headache. Comprehensive data are provided in **Tables 1 and 2**.

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Table 2. Infusion rate of HES and ICP average values per day in epidural HES infusion therapy.

	Case					
	Case 1		Case 2		Case 3	Case 4
	HES infusion rate (mL/h)	Mean ICP±SD (mmHg)	HES infusion rate (mL/h)	Mean ICP±SD (mmHg)	HES infusion rate (mL/h)	HES infusion rate (mL/h)
After surgery		1.56±1.38		2.45±2.11		
Day 1	6	4.61±0.83	6	4.29±1.37	3	3
Day 2	6	7.10±1.31	6	4.21±2.11	3	3
Day 3	3	8.23±0.64	3	6.45±3.18	3	3
Day 4	3	7.69±1.43	6	9.07±2.22	1	
Day 5	1	8.55±1.65	3	7.79±1.96	1	
Day 6			1	15.81±3.94		
Day 7			1	9.12±1.86		

Abbreviations: HES, hydroxyethyl starch; ICP, intracranial pressure; SD, standard deviation.

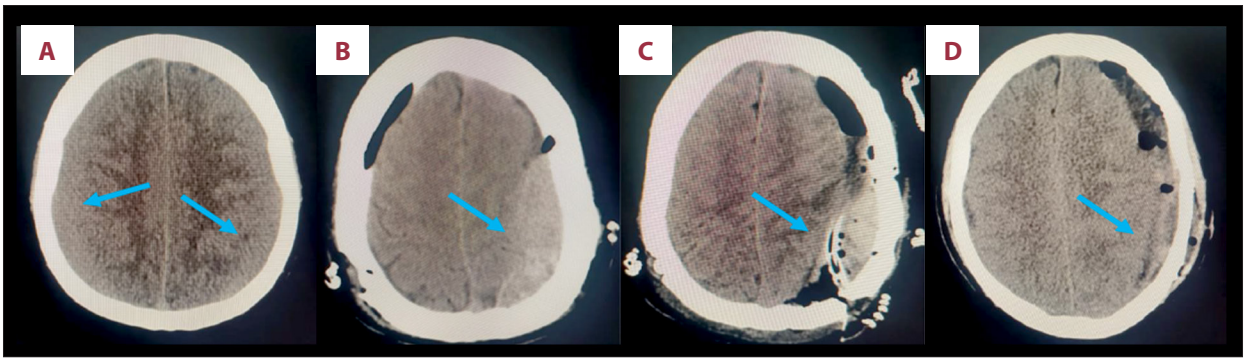

Figure 2. (**A**) Preoperative brain CT showing bilateral frontoparietal and temporal chronic SDHs (blue arrow; maximum thickness of SDH: 13 mm). (**B**) Brain CT on postoperative day 1 indicating postoperative changes of bilateral SDHs with persistent left frontoparietal epidural and subdural collections (blue arrow). (**C**) Brain CT on postoperative day 2 illustrating interval improvement in bilateral SDHs, with further reduction of the left frontoparietal epidural and subdural collections compared with those in the anterior regions (blue arrow). (**D**) Brain CT at discharge showing no new hematoma formation (blue arrow).

Discussion

HES has emerged as a promising therapeutic modality in the management of PDPH and SIH [11,13]. Specifically, a single epidural injection of 20 mL HES has been documented as a successful treatment for SIH without complications [11]. The efficacy of HES may be mediated by its ability to increase epidural pressure, thereby generating a mechanical tamponade effect that reduces CSF leakage [15]. However, the elevation in epidural pressure achieved with a single HES injection appears to be short-lived, which may limit the durability of its therapeutic benefit [15]. Additionally, the continuous epidural infusion of liquids over 24 to 48 h through an epidural catheter may contribute to spontaneous healing [16], as demonstrated in a study in which continuous epidural infusion of HES for 2 days was shown to prevent PDPH [13]. The rationale behind continuous epidural fluid infusion is to reduce the pressure gradient between the intrathecal and epidural spaces, thereby promoting spontaneous fistula closure by limiting CSF leakage into the epidural space [10]. Compared with continuous epidural saline infusion, which is rapidly redistributed and therefore produces only short-lived increases in epidural pressure without directly sealing the dural defect[17-19], HES infusion can provide a more sustained therapeutic effect owing to its longer persistence in the epidural space. This prolonged epidural persistence may help maintain pressure modulation and mechanical tamponade at the site of CSF leakage [16]. Epidural blood patching promotes closure of the dural defect through clot formation [7], whereas HES infusion likely exerts its therapeutic effect primarily through sustained epidural pressure

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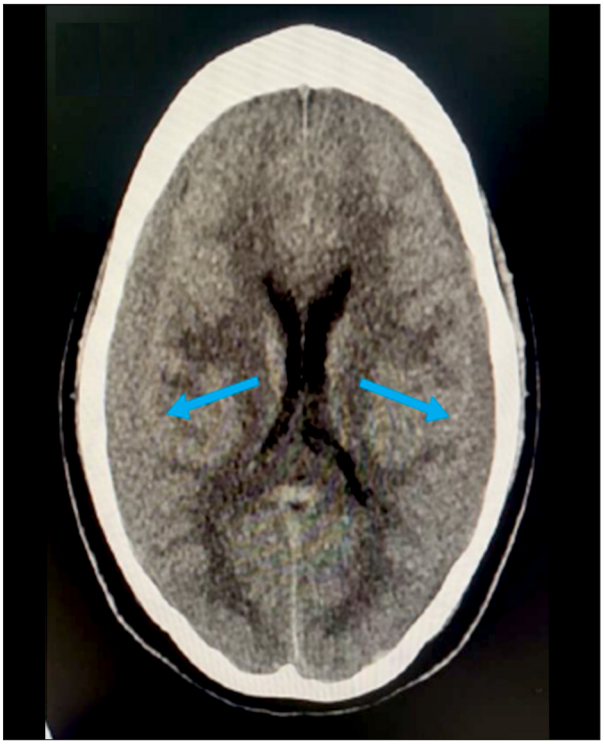

Figure 3. Brain CT scan before discharge revealing bilateral frontoparietal and temporal subdural effusions (blue arrow).

modulation and mechanical tamponade rather than by direct sealing [16]. These differences may partly account for the favorable outcomes observed in our 4 patients. However, reports specifically evaluating continuous epidural infusion of HES for SIH remain limited, highlighting the need for further investigation.

In the prophylaxis of PDHD using HES, an epidural infusion rate of 6 mL/h has been described [13]. This rate or lower was used in our cases, and these consecutive infusions were successful. Among the 2 patients who underwent SDH evacuation, we observed marked improvement in low ICP following epidural infusion of HES, suggesting that adjusting HES infusion rates and duration based on ICP measurements is safe and effective. The infusion parameters used in the other 2 patients were extrapolated from the experience gained in the first 2 cases and were likewise safe and effective. On this basis, we now restrict the duration of continuous epidural infusion to a maximum of 7 days to minimize the risk of neuraxial infection and cap the infusion rate at 6 mL/h. If there are symptoms suggestive of intracranial hypertension (eg, nausea, vomiting, or headache) during the infusion, the infusion rate is immediately reduced or the infusion is discontinued. However, in the absence of ICP monitoring, determining the optimal infusion rate and duration for epidural infusion of HES in SIH patients with different complications remains challenging and warrants further investigation.

Notably, previous human and animal studies involving epidural HES injection have not documented neurologic adverse effects [13,20,21]. In our cohort, all 4 patients demonstrated favorable clinical responses without recurrence, rebound intracranial hypertension, or adverse neurological events during treatment or follow-up. Nonetheless, 1 patient developed left lumbar and hip pain, and another experienced catheter dislodgement, prompting further consideration of potential complications and overall safety. A major limitation of our study is the small sample size, underscoring the need for larger clinical series and prospective studies to clarify the precise mechanisms, efficacy, potential complications, and long-term prognosis associated with continuous epidural infusion of HES.

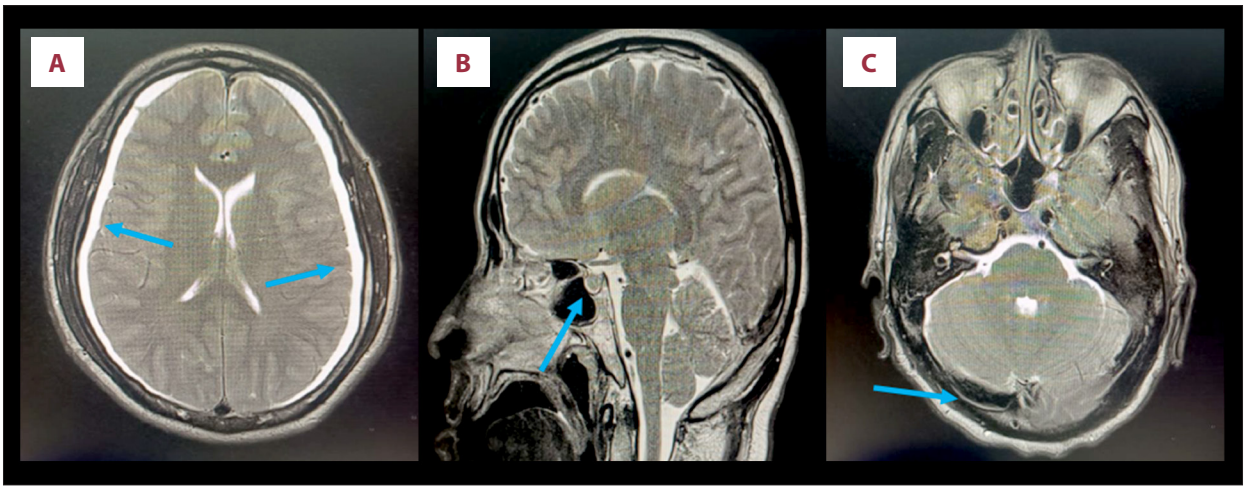

Figure 4. Brain T2-weighted MRI showing (**A**) bilateral subdural effusions in large cerebral hemispheres (blue arrow), (**B**) slight swelling of the superior pituitary margin (blue arrow), and (**C**) subtle dilation of the venous sinuses (blue arrow).

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Conclusions

SIH should be strongly considered in patients with SDH who present with orthostatic headache or lack a history of head trauma. In selected patients undergoing evacuation of non-traumatic SDH, subdural intracranial pressure monitoring can be a useful adjunct in the diagnosis and management of SIH. Within this clinical context, the positive outcomes observed in our cases support continuous epidural infusion of HES as a potentially effective epidural pressure-modulating strategy for correcting low ICP and suggests its utility in the management of SIH.

Departments and Institution Where Work Was Done

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Patient Consent Statement

Written informed consent was obtained from all patients.

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AI Disclosure

No artificial intelligence (AI) tools were used in the preparation of this manuscript.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

Abbreviations

SIH, spontaneous intracranial hypotension; **CSF**, cerebrospinal fluid; **SDH**, subdural hematoma; **EBP**, epidural blood patching; **HES**, hydroxyethyl starch; **MRI**, magnetic resonance imaging; **CT**, computed tomography; **ICP**, intracranial pressure; **AI**, artificial intelligence.

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