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Spontaneous hypertensive brainstem hemorrhage: Does surgery benefit the severe cases?

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ABSTRACT

Background: Treatment of hypertensive brainstem hemorrhage (HBSH) is still controversial, especially for severe cases (GCS ≤ 8). With the improvement in neuroimaging and microsurgical techniques, severe HBSH is no longer considered inoperable. We analyzed comatose patients in whom radiology revealed severe HBSH. We further analyzed the outcome of cases we successfully operated on and compared surgical intervention with conservative management.
Methods: We retrospectively analyzed data obtained from patients with HBSH who represented at our facility from 2005 to 2015. We evaluated their demographics data, lesion characteristics, surgical approaches, as well as outcomes. We further assessed their outcomes with the Glasgow Outcome Scale (GOS). We also compared the outcome of surgical hematoma evacuation with conservative treatment.
Results: A total of 286 adult patients with severe HBSH was included in the study. Forty-six (46) patients were treated via craniotomy and the evacuation of the hematoma within 3 h to 2 days on admission at the emergency department. Ultra-early surgery (within 6 h of ictus) was performed in twenty (20) cases (43.5%). 240 patients were managed conservatively. The mortality rate for surgical group was 14/46 (30.4%) while the conservative group was 169/240(70.4%). The timing of surgical intervention was one of the strongest factors affecting outcome GOS ($p = 0.02$). The volume of the hematoma, GCS score on admission and the presence of acute hydrocephalus also affected the outcome ($p = 0.03$ respectively).
Conclusions: Our data suggest that early surgical intervention is very crucial in achieving successful outcomes in patients with severe HBSH.

1. Introduction

Brainstem hemorrhage was first identified by Cheyne in 1812 during his work on apoplexy and lethargy which he published in London [1]. The abnormal breathing pattern described in his publication is currently referred to as Cheyne–Stokes respiration. However, it is Mangiardi who further distinguished hypertensive brainstem hemorrhage (HBSH) from other brainstem hemorrhagic disorders in 1988 during his work on brainstem hematomas [2]. According to Mangiardi, HBSH is defined as a diffuse brainstem hemorrhagic lesion occurring in an elderly patient. It is usually associated with systemic hypertension instead of brainstem cavernous malformation (BSCM). It often resulted in profound, irreversible neurological deficits as well as high fatality rate. Therefore, patients who presented with HBSH were often not fit for surgery and thus managed conservatively. However, conservative management still carries a high mortality and morbidity rate. A recent study by Wang et al. [3] in 2011 with 102 cases revealed that the mortality rate of HBSH is as high as 69.61% with conservative management.

With the advent of modern neuroimaging methods and microsurgical techniques, the burdens of both diagnosis and therapeutics have become considerably lighter [2]. Since Lassiter's first surgical exploration of suspected lesions in the brainstem [4], a number of neurosurgeons have successfully operated and drained unsuspected brainstem hematomas [5–7]. However, no one has purposefully attempted to operate on HBSH cases, not to mention severe cases. Severe HBSH (Glasgow coma scale (GCS) ≤ 8) constitutes a very special subgroup because of the associated high mortality rate and uncertainty of the best therapeutic approach. Those patients were traditionally considered inoperable and thus unsalvageable. The purpose of this report is

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to present our preliminary clinical experience with 286 patients who suffered severe HBSH. We also discussed the management of this unique disease entity.

1.1. Aims and objectives

Treatment of hypertensive brain stem hemorrhage (HBSH) is still controversial, especially for severe cases (GCS ≤ 8). With the improvement in neuroimaging and microsurgical techniques, severe HBSH is no longer considered inoperable. Therefore, we analyzed comatose patients in whom radiology revealed severe HBSH. We further analyzed the outcome of cases we successfully operated on and compared surgical intervention with conservative management. We noticed that surgical intervention carries a good prognosis if the decision is taken within 6 h after the HBSH.

2. Patients and methods

Clinical data was obtained from 286 adult patients with brainstem hemorrhage as a result of hypertension from 2005 to 2015. The Institutional Review Board at West China Hospital and Medical Center approved this study. Exclusion criteria included suspected cavernomas on preoperative imaging; the hemorrhage was probably due to an aneurysm or an angiographically proven arteriovenous malformation; the hemorrhage was secondary to a tumor or trauma; and those who didn't have hypertensive history. Also excluded were those patients whose Glasgow Coma Scale (GCS) score > 8. Any case in which proper modern imaging techniques (CT or MRI) were unavailable was also excluded from the study, so that all cases included in the study comply with modern standards of medical care. For the purpose of data analysis, the brainstem was divided into the following segments: midbrain, pontomesencephalic junction, pons, pontomedullary junction, and medulla. Lesions located entirely within the thalamus or basal ganglia were excluded, but lesions extending into the thalamus from the midbrain were included.

All patients included in the study were offered the option of surgery. Their relatives either agreed for surgical intervention or refused surgery. Those patients whose family consented the surgery were allocated to surgery group, and those whose family refused the surgery were put into the conservative treatment group. In all surgery cases, somatosensory evoked potentials as well as motor evoked potentials were monitored. Follow-up was obtained from relatives and care providers, at the outpatient department, by telephone, or in a questionnaire response to written inquiries.

Hematoma volume was determined in the A × B × C/2 manner [8–10], in which the largest diameter (A) of the hematoma was measured with centimeter scale on the CT film. The diameter of the hematoma perpendicular to the largest diameter represented the second diameter (B). The height of the hematoma was calculated by multiplying the number of slices involved by the slice thickness, this constitutes the third diameter (C). Primary outcome using the Glasgow outcome scale six (6) months after ictus was either death or disability. Secondary outcomes were also assessed using the modified Rankin scale. We used Statistical Package for the Social Sciences software (version 22.0) (SPSS, Chicago, IL, USA) to do the analyses. During our analyses, $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patient features

Out of the 286 patients included in the study, 46 were operated on while 240 were managed conservatively (Table 1). Most of the patients presented with sudden-onset of symptoms. Patients' neurologic deficits were typically pronounced and permanent. The location of the hematoma was usually the brainstem (Fig. 1: 1; A, B and 2; A, B). Presenting signs and symptoms correlated with expected neurological deficits based on the anatomical location of the lesion in the brainstem. Increased intracranial pressure (ICP) was most often observed in midbrain cases. Cranial nerves V-VIII palsy and hemiparalysis were more commonly seen in pontine lesions. Cardiovascular and respiratory instability and dyspnea were more prevalent in patients with medullary hemorrhage. The triggers in most patients were mostly identified to be emotional surge, and vigorous exertion at work or house chores. About 15% of the patients were playing Mahjong, a popular game widely played throughout Eastern and South-Eastern Asia, at the time. There were no apparent triggers or the triggers could not be clearly identified in 34.5% patients. With Regard to the past medical history of the patients we operated on, 15(32.6%) of them had previous myocardial infarction while 8(17.4%) of them had previous stroke. The remaining patients had no obvious past medical history or risk factors.

Table 1
Baseline characteristics of patients.

	Surgery group(n = 46)	Conservative management(n = 240)
Age(years)		
Median(IQR;range)	52(36–80)	51(31–85)
Mean(SD)	51.5	53
< 60	26(56.5%)	167(69.6%)
60–69	8(17.4%)	47(19.6%)
≥70	12(26.1%)	26(10.8%)
Sex		
Male	35(76.1%)	174(72.5%)
Female	11(23.9%)	66(27.5%)
Glascow Coma Score		
3	15(32.6%)	70(29.2%)
4	6(13%)	40(16.7%)
5	15(32.6%)	72(30%)
6	4(8.7%)	29(12.1%)
7	1(2.2%)	2(0.8%)
8	5(10.9%)	27(11.2%)
Medical history		
Previous myocardial infarction	15(32.6%)	57(23.8%)
Previous stroke	8(17.4%)	102(42.5%)
Medication before ICH		
Anticoagulant drugs	7(15.2%)	45(18.8%)
Antiplatelet drugs	11(23.9%)	67(27.9%)
Thrombolytic drugs	12(26.1%)	89(37.1%)
antihypertensive drugs	30(65.2%)	156(65%)

Hematoma Features.

On preoperative images, pontine hematoma was the most common. We detected pontine hematoma in 21 cases in the surgical group and 123 cases in the conservative group. Ventricular extension of hematoma was also observed in about half of the cases we operated. Furthermore, only 18 cases presented with radiographic hydrocephalus which was mostly seen at the upper pons and medullary levels in 90 cases (84.1%). (Table 2).

3.2. Management

Eventually, 46 patients underwent surgical evacuation, whereas the remaining 240 patients were managed conservatively. The surgical approaches were implemented as follows: hematomas at the tectum of mid-brain were removed through Poppen's suboccipital transtentorial approach (n = 4); those reaching the lateral surface of the midbrain were managed by subtemporal-tentorium approach (n = 10); Suboccipital retrosigmoid approach was used to access ventrolateral lesions of the pons (n = 20), and posterior fossa midline approach for dorsal pontine and medullary lesions (n = 12) (Table 2). The mean duration of preoperative clinical history was 12 h (3 h to 2 days). Ultra-early surgery (within 6 h of ictus) was performed in 20 cases (43.5%)

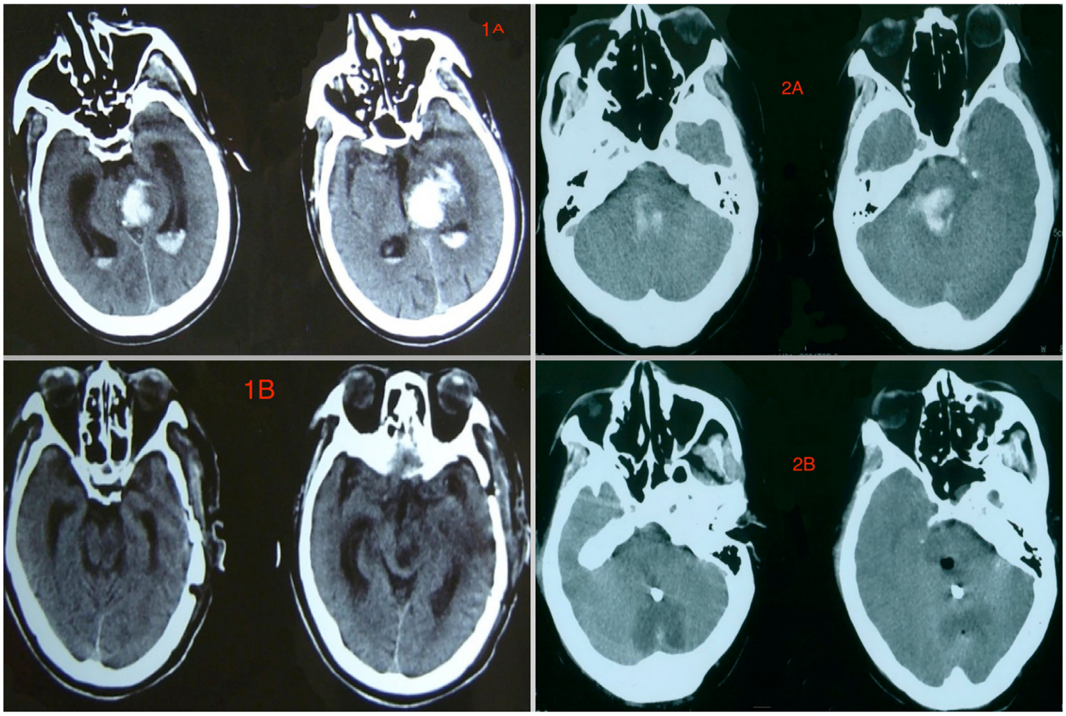

Fig. 1. 1–A, B and 2–A, B are CT-Scan images showing the location of the HBSH. 1A and 2A are preoperative images while 1B and 2B are postoperative images.

Table 2
Characteristics of haematomas.

	Surgery group(n = 46)	Conservative management(*n* = 246)
Volume (mL)		
Median (IQR; range)	8.5	8.6
Mean (SD)	8.7(0.5)	8.9(0.7)
Site of hemorrhage		
Mesencephalic	12(26.1%)	42(17.5%)
Pontomesencephalic	3(4.3%)	25(10.4%)
Pontine	21(47.8%)	123(51.3%)
Pontomedullary	4(8.7%)	32(13.3)
Medullary	6(13%)	18(7.5%)
Hydrocephalus		
Yes	18(39.1%)	89(37.1%)
No	28(60.9%)	151(62.9%)

Table 3
Details of surgical approaches we used during operation.

	Surgery group (n = 46)
Approach	
Poppen's approach	4(8.7%)
Subtemporal-tentorium approach	10(21.7%)
Suboccipital retrosigmoid approach	20(43.5%)
Posterior fossa midline approach	12(26.1%)
Time from ictus to surgery (h)	
Median (IQR; range)	11
Mean (SD)	12(0.5)
Surgery within 6 h of ictus	20

(Table 3). 24 cases operated between 6 and 48 h. 2 cases were operated after 48 h. Operative approaches were selected based upon the location of hematoma and where hematoma reached the brain stem surface. CT-Scan guided neuronavigation was utilized in all case that were operated on to locate the hematoma. Intraoperatively, we monitored sensory evoked potentials (SEPs) to evaluate the integrity of ascending sensory tracts while and motor evoked potentials (MEPs) to evaluate the functionality of descending motor pathways. We further divided the SEP into three clinical modalities such as: somatosensory (SSEP), auditory (BAEP), and visual (VEP). The analysis is however not included in our results. We suggest further studies on HBSH be geared toward this direction. In cases with ICP, ventriculo-peritoneal shunts were passed and revised when we notice blockade.

3.3. Outcomes

Follow-ups of the patients we operated on were via routine outpatient department visits or via telephone interview or written correspondence from relatives or care provides from 6 months to 8 years (average, 4.5 years). We however did not loss any patient on follow-ups. The mortality rate of the surgical group was 14/46 (30.4%) while the conservative group was 169/240(70.4%). 6 cases (13.1%) achieved good recovery in the surgery group whereas the recovery rate was only 5.9% (14/240) in the conservative group. The major complication in both groups was stress ulcers and pneumonia. However, CN nerve palsy was commonly seen in 62.9% of the conservative group as compare to 36.9% in the surgical group. Furthermore,54.3% of the surgical group had miscellaneous complications such as bed sores and deep venous thrombosis (Table 4 and Fig. 2). A detailed analysis of preoperative parameters associated with patient outcome revealed that the volume of the hematoma, time of surgery, GCS score on admission and the presence of acute hydrocephalus had significant effects on the outcome ($p < 0.05$ respectively) (Table 5).

4. Discussion

HBSH is not uncommon, especially in eastern Asian populations. It accounts for approximately 10% of the intracerebral hemorrhage (ICH) [11]. It has a very high morbidity and mortality rate due to the critical anatomic location of the hematoma. The reported mortality rate for patients with hematomas larger than 5 ml is as high as 80–100% [12]. However, its exact etiology is still shrouded in mystery and misunderstanding, which resulted in the many controversies surrounding

Table 4
Complications associated with management of patients.

	Surgery group(n = 46)	Conservative management(n = 240)
GOS		
Death	14(30.4%)	169(70.4%)
Vegetative	2(4.3%)	6(2.5%)
Severe disability	15(32.6%)	32(13.3%)
Moderate disability	9(19.6%)	19(7.9%)
Good recovery	6(13.1%)	14(5.9%)
Rankin		
0	5(10.9%)	12(5%)
1	2(4.3%)	15(6.3%)
2	4(8.7%)	18(7.5%)
3	10(21.7%)	17(7.1%)
4	5(10.9)	4(1.7%)
5	6(13%)	5(2.1%)
Dead	14(30.4%)	169(70.4%)
Mortality at 6 months		
Dead	14(30.4%)	169(70.4%)
Live	32(69.6%)	71(29.6%)
Complications		
Stress ulcer	12(26.1%)	57(23.8%)
Pneumonia	14(30.4%)	89(37.1%)
CN palsy	29(63%)	95(39.6%)
Others	6(13%)	133(55.4%)

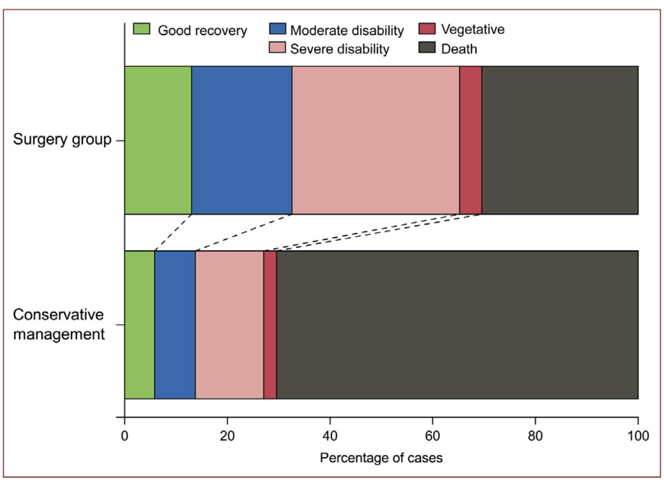

Fig. 2. is a graphical representation of complications associated with management of patients.

the management. Mangiardi's suggested that HBSH was a very different disease entity from BSCM [2]. Thus, principles in the management of BSCM may not apply in the settings of HBSH. This study was therefore conducted to provide an in-depth analysis of our experience with 286 severe HBSH cases. Our focus was on 46 cases whom we successfully operated with a good outcome.

We agree that not every HBSH case requires surgical intervention. Our data reflected that even in the settings of a high-volume tertiary center, significant morbidity and mortality were potentially associated with the treatment of HBSHs. Nevertheless, surgical evacuation of HBSHs may be warranted in appropriately selected patients; that is, patients with (1) severely disrupted vital signs, especially those with shallowed breathing (Cheyne-Stokes) and central hyperthermia (2) Volume of the hematoma > 5 ml (3) GOS < 8 (4) The distance from the brainstem surface to the hematoma < 1 cm. Although the morbidity associated with surgical management is significantly high as 30.4%, we believe our results demonstrate that surgical outcomes may be satisfactory in carefully selected patients. This is especially true for

Table 5
Outcomes of surgical patient stratified by preoperative parameters.

Variable	GOS				*P* Value
	Improved		Same or worse		
	No.	%	No.	%	
Age, y	52.5 ± 8.0		53 ± 10.6		.79[a]
Sex					.92[b]
Male	14	66.7	17	68	
Female	7	33.3	8	32	
Volume, ml	7.3 ± 2.4		8.4 ± 3.3		.03[a]
Location					.79[b]
Mesencephalic	6	28.6	6	28.6	
Pontomesenchephalic	2	9.5	1	4.8	
Pontine	10	47.6	11	52.4	
Pontomedullary	1	4.8	3	14.3	
Medullary	2	9.5	4	19	
Time from onset to surgery, h					.02[b]
≤6	13	61.9	7	28	
> 6	8	38.1	18	72	
GCS (on admission)					.03[b]
3	1	4.8	1	4.8	
4	2	9.5	11	52.4	
5	6	28.6	6	28.6	
6	8	38.1	6	28.6	
7–8	4	19	0	0	
Hydrocephalus					.03[c]
Yes	12	57.1	6	24	
No	9	42.9	19	76	

[a] Unpaired *t*-test (presented as mean ± standard deviation).
[b] X^2.
[c] Fisher's exact test.

the severe cases, as indicated by other authors [5,13], because the resultant hemorrhage may lead to severe destruction of the brainstem resulting in poor prognosis. The even higher mortality rate (70.4%) in the conservative group served as a powerful remainder that conservative management may not be the best treatment for those patients.

In our study, 20 cases were operated within 6 h after the ictus. 13 of them (61.9%) achieved better neurological functions during the follow-up period after the surgery, which is a significant improvement as compare to 38.1% of improvement rate in the late operative group (> 6 h) (p = 0.02, Table 5). This may indicate that although it is fragile the brainstem has tremendous compensation capacity. The neurologic deficits observed right after the ictus might be partially reversible if early surgical evacuation was available at an early stage. Animal studies also reveal that the edema and arterial necrosis usually begin and exacerbate the symptoms 6 h after the initial hemorrhage in the brainstem [14]. Therefore, we advocate that surgical intervention should be carried out within 6-hour time window whenever possible.

The overall mortality of the cases we operated on was 30.4%, which was significantly lower than that of conservative management group (70.4%). However, the morbidity rate seemed to be higher than the conservative group with 32.6% of severe disability rate. We postulated this was most likely due to fact that the surgical group may have time to show more neurological deficits than the conservative group because of their prolonged survival time. Similar phenomenon was reported in other stroke cohorts as well [15,16]. In addition, we also found out that patients harboring lower brainstem hemorrhage had poorer outcome. This was probably contributed to the early onset of breathing dysfunction after the ictus, which was more commonly seen in medullary hemorrhage [17–19]. However, the analysis of our study failed to find any significant difference in terms of the relation between the location and outcome (p = 0.79).

Hematoma volume is a powerful predictor of clinical outcome in patients with HBSHs (p = 0.03). Hematoma volume adds to intracranial volume and may cause life-threatening elevation of intracranial pressure [20]. The hematoma volume was > 10 ml in 7 patients and five of them had worse neurological outcome after surgery, in which three patients passed away eventually. In a number of studies, a fatal or poor outcome was reported in patients with poor GCS score on [21–23]. In accordance with these results, the present study also showed that a low GCS score was related to worse outcomes ($p = 0.03$).

Considering the radiological findings, some authors have suggested that intraventricular extension is associated with bad outcome [21,24]. However, we found out that acute hydrocephalus was associated with good outcome in 57.1% of cases with improved outcome ($p = 0.03$), whereas intraventricular extension didn't have a role. Additionally, the percentage of better surgical outcome in the hydrocephalus group was better than that of none hydrocephalus group (57.1% vs 42.9%). We therefore postulate that hydrocephalus was partially responsible for the neurological deterioration in patients with hydrocephalus. We managed cases of such hydrocephalus by passing ventriculo-peritoneal shunt. Surgical evacuation not only removed the hematoma but also provided a relief for the hydrocephalus. However, this theory remains to be tested in larger series of cases.

5. Conclusions

In this study, we analyzed the surgical outcome of 46 severe patients (GCS ≤ 8) with spontaneous HBSH whom we operated on. The survival rate with minimal or severe disability for surgical group was 32/46 (69.6%). Which means that early surgical intervention is beneficial to patients with HBSH. This is the first single large tertiary center's study in literature. We propose that further studies with larger data are still needed to arrive at more effective management regimens for this subclass of intracerebral hemorrhage.

Declaration of conflict of interest

All the authors declare no conflict of interest.

Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

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